BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or payper-view fees (http://bmjopen.bmj.com).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

BMJ Open

Modeling Diabetes and Related Medical Care of the Future Elderly in Mexico

Journal:	BMJ Open
Manuscript ID	bmjopen-2017-017330
Article Type:	Research
Date Submitted by the Author:	04-May-2017
Complete List of Authors:	Gonzalez Gonzalez, Cesar; Universidad de Colima, Facultad de Trabajo Social Tysinger, Bryan; University of Southern California Goldman, Dana; University of Southern California Wong, Rebeca; University of Texas, Department of Preventive Medicine and Community Health
 Primary Subject Heading :	Diabetes and endocrinology
Secondary Subject Heading:	Public health, Health economics
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, HEALTH ECONOMICS, PUBLIC HEALTH

SCHOLARONE™ Manuscripts

Modeling Diabetes and Related Medical Care of the Future Elderly in Mexico

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

School of Social Work, University of Colima, Mexico, Cesar Gonzalez-Gonzalez professor Roybal Center for Health Policy Simulation, University of Southern California, Bryan Tysinger director

Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Dana P Goldman director,

Sealy Center on Aging, University of Texas Medical Branch, Rebeca Wong professor

Corresponding author: C Gonzalez-Gonzalez cgonzalez31@ucol.mx

Abstract

Objective Mexico is experiencing one of the fastest aging processes in the world. Diabetes represents a major health problem and a significant burden on the population and on health systems. Diabetes is associated with an increased risk of hospitalization, co-morbidity and mortality. Given these health conditions and the complex socioeconomic scenario of developing countries like Mexico, the goal of the study was to estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes.

Design A simulation study using data from three waves (2001, 2003 and 2012) of the Mexican Health and Aging Study (MHAS) and adapting the Future Elderly Model (FEM) to simulated four scenarios for the projected diabetes prevalence rates among population 50 years and older.

Participants Data from 14,662 participants with information on mortality, self-reported diabetes, and health and demographic characteristics.

Outcome measures For each scenario of diabetes incidence reduction, we calculated summary measures for population aged 50 and older from 2012-2050 in two year increments: Prevalence of diabetes, Total Population with diabetes, Number of medical visits.

Results In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico, 19.3% had been diagnosed with diabetes and the 2001-2003 diabetes incidence was 4.3%. The no-intervention scenario shows that the prevalence of diabetes is projected to increase from 19.3 to 34.0%, under the 30% reduction scenario the prevalence of diabetes will be 28.6%. When comparing the no-intervention scenario versus the 30% and 60% diabetes incidence reduction scenarios we calculated for the year 2020 a total of 816,320 and 1.6 million annual averted cases of diabetes.

Discussion Our study underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions.

Strengths and limitations of this study

- The study is the first in Mexico using longitudinal-individual data to project the prevalence of diabetes among older adults in Mexico.
- The study uses an adapted version of the Future Elderly Model, a demographic and economic simulation model designed to project the future costs and health status of the elderly based on their current health status and taking into account a broad set of risk factors.
- Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in total population with diabetes.

Introduction

Diabetes represents a major health problem and a significant burden on health care systems and societies overall. This is particularly the case in countries like Mexico, whereas the prevalence of diabetes among the population 20-79 years old was 15.9% in 2011. This was the highest in the OECD (1) and ranked No. 9 worldwide (2). According to the national estimates in Mexico, the self-reported prevalence of diabetes among population aged 60 and older was 24% in 2012, and in the period between 2000 and 2012 the prevalence doubled among those aged 70 and older from 10 to 20%, and among those aged 60-69 the prevalence grew 1.5 times, going from 18 to 26% (3).

Population aging and the growing prevalence of diabetes raise concerns among the social, health and family systems because of the known consequences of this disease. People with diabetes may experience additional health complications (4) (5), greater social needs (6), loss in productivity and earnings (7) and diminished quality of life (8) (9). Moreover, in 2012, diabetes was the leading cause of mortality in the Mexican adult population, with 17% of all deaths. It is also the leading cause of premature withdrawal from economic activity, blindness and renal failure. Overall, diabetes has a direct impact not only on life expectancy overall but also the quality of life of the older adult population.

A key risk factor associated with diabetes is high body weight (10), as obese or overweight individuals are more likely to become diabetic (11). Estimates from the 2012 National Health Survey in Mexico reveal that 41% of adults aged 30-49 were overweight, 37% obese and 79% had abdominal obesity, and the figures are similar for those aged 50 years and older (3). Furthermore, obesity is projected to increase across all age groups with serious present and future implications for diabetes patients and for the Mexican health care system (12).

From a public policy perspective, it is important to take a glance into the future burdens and understand how the prevalence of diabetes will change over the next decades. Moreover, since there are health interventions that have proven to be effective in reducing the onset and management of the disease, it is important to understand how current and potential new policies, particularly those designed to prevent or ameliorate the rise of chronic diseases may alter the

diabetes trends. For sure, the future prevalence of diabetes will be influenced by the momentum of population aging, the trends in obesity, and the patterns of medical advances, among others. Thus, we estimate future trend of diabetes among older adults in Mexico, assuming the current patterns of risk factors and behaviors, as well as the likely trends if preventive measures were adopted to reduce the onset of new cases.

One way to assess the future burden of the disease is to use microsimulation models. Projecting the prevalence of diabetes, the number of diabetics in the population, and the consequences for the health care system in terms of health care needs, can be useful for public health policy makers, in order to raise awareness of the potential consequences of varying paths that the burden of diseases can take, and possibly designate resources to prevent cases. Microsimulation has been used as a tool for social science research and policy analysis(13), and can be used to evaluate the impact of interventions under alternative scenarios (14). Such scenarios often rely on information from clinical trials where evidence strongly supports that the onset of a disease is preventable or could be delayed. For example, a systematic review of the literature concludes that a variety of interventions can help reduce the onset and improve the management of diabetes in a diversity of country settings. This review takes into account the costs involved as well (15). To illustrate for the United States, the Diabetes Prevention Program (DPP) was a multicenter randomized clinical trial that demonstrated that weight loss through dietary changes and more physical activity could prevent or delay onset of Type 2 diabetes. The DPP also showed that use of a generic oral diabetes drug (metformin) could reduce the incidence of disease among at-risk individuals. Thus, for the purposes of this paper, we consider what the future prevalence of diabetes might be if it were possible to adopt public health interventions that reduced the incidence of diabetes on a scale up to the results shown by the DPP (16). While we assume average effectiveness of national-level interventions and these levels may be difficult to achieve, the assumed scenarios can help policy makers to understand the impact on the burden of diabetes if these various levels of prevention could be achieved, including what the projected burden would be if no interventions were adopted.

We estimate future levels of diabetes under different scenarios for the population aged 50 years and older in Mexico. If interventions were to be implemented to reduce the incidence of

diabetes, how much would the prevalence of diabetes change? And how would the economic burden of diabetes diminish, in terms of medical resources to treat the disease? To address these questions we modeled the trajectory of future diabetes in Mexico from 2012 to 2050 using the Future Elderly Model (FEM), a microsimulation model. We constructed four scenarios for the projections, estimating the effect of reducing 2-year diabetes incidence rates by 0%, 10% 30% and 60%. In order to estimate prevalence of diabetes among the population aged 50 and older in the future, we take into account the current prevalence, the estimated new cases of diabetes (incidence) among those aged 50 and older in each 2-year period, the deaths among the group 50 and older in each 2-year period, and the prevalence among new population entering the group 50 and older in each 2-year period in the future. The microsimulation model takes these components into account.

Methods and data

The FEM is a demographic and economic simulation model, originally designed to project the future costs and health status of the elderly based on their current health status and taking into account a broad set of risk factors (17). In contrast to projection models that use aggregate measures of health traits for a population cohort, the FEM uses information on how individual health characteristics change at the individual level using longitudinal survey data (18). FEM details have been described elsewhere (19).

To estimate the future burden of diabetes in Mexico using the FEM, we use data from the Mexican Health and Aging Study (MHAS), a prospective survey of a nationally and urban–rural representative sample of adults aged 50 years and older residing in Mexico in 2001 (20). From its inception, the MHAS was designed to be highly comparable to the U.S. Health and Retirement Study (HRS). The MHAS content includes health in multiple domains, health behaviors and risk factors, socioeconomic conditions, work history, health insurance, health expenditures, and family background, among others. A next-of-kin module gathers information on deceased study participants. The MHAS has three waves of available data (2001, 2003, and 2012). A refresher sample of individuals aged 50-60 was added in 2012, to once again represent the population aged 50 and older in 2012.

For our purposes, FEM-Mexico uses two main modules of the FEM developed for the U.S. (FEM-US). The first produces individual trajectories, that is, transitions, and estimates incidence for a number of health conditions and disability statuses. The second module ensures that the data remains representative of the population aged 50 years and older by replenishing the sample every two years, with 50-51 year olds incorporated to the sample every two years.

The data used for the FEM-US and the FEM-Mexico differ in one important methodological aspect, the inter-wave periods. As mentioned above, the FEM was created to be used with the U.S. Health and Retirement Study (HRS), a longitudinal survey collected every two years; MHAS has a two-year gap between the first (2001) and second (2003) wave, and a 9-year gap between the second and third (2012) wave. To overcome this methodological difference we use the MHAS 2001 and 2003 waves to estimate health transitions and estimate 2-year incidence, and we use the 2012 wave as the baseline to start the microsimulation. In other words, we impose the 2001-2003 health transitions to the 2012 MHAS population. We tested the adequacy of this approach by applying the 2001 prevalence and the 2001/2003 incidence to project the estimated prevalence of diabetes in 2012. We then compared the estimated prevalence with the observed prevalence in MHAS 2012 and the estimates were quite similar, hence we concluded that this approach is reasonable. These results are not shown but are available from the Technical Appendix.

To measure diabetes prevalence, MHAS respondents were asked: 'Has a doctor or medical personnel ever told you that you have diabetes or a high blood sugar level?' The equation for the 2001 to 2003 diabetes incidence estimates the probability of developing diabetes, using a probit regression model with covariates that are characteristics measured in 2001 as follows: age (50-64, 65-74, 75+), gender (male, female), education (less than basic, basic, high school and college), marital status (single, married, separated/divorced, widowed), ever hypertension (yes, no), body mass index (BMI underweight/normal, overweight, obese¹), smoking status (never, current, or former), physical activity in the last two years (yes/no), size of locality of residence (less than 100,000 inhabitants, and 100,000 or more inhabitants) and health

¹ Underweight/normal is defined as a BMI lower than 25, overweight is defined as a BMI between 25.0 and 29.9, and a BMI of 30 or higher is considered obese.

insurance (yes/no). To estimate the incidence equation, only the cases that report no diabetes in 2001 are included in the analytical sample.

We estimated similar incidence equations using probit regression models for self-reported hypertension, cancer, heart attack, lung disease, stroke, and for mortality; ordered probit models for smoking status (never, current, former), limitations with five Activities of Daily Living (ADL's) (none, one, two, three or more) and four Instrumental Activities of Daily Living (IADL's) (none, one, two or more) and linear regression models for log (BMI). The list of variables included in the right-hand-side of each equation varies depending on the theoretical relationship of the independent variables with the corresponding dependent variable.

Since FEM works as a simultaneous equations model, the parameters in one equation affect the parameters of the other equations, meaning that transitions could occur in multiple diseases in any given year of the projection. Thus, an individual could have more than one disease transition in the same year, e.g. new diabetes and new hypertension. Similar to FEM-U.S., in FEM-Mexico once a health condition (chronic disease) is acquired or mortality occurs, these states are treated as absorbing or permanent.

In addition, we assessed the economic consequences of diabetes by comparing the number of medical visits by diabetics *versus* non-diabetics. We estimated an OLS equation for the number of medical visits as dependent variable, including with/without diabetes as the main explanatory variable. MHAS respondents were asked: 'In the last year, how often have you visited or consulted a doctor or medical personnel?'

To maintain representativeness of the 50 year and older population, the microsimulation model needed replenishment cohorts every two years. To replenish the sample we took the sample of 50/51 year olds that were added to the sample from MHAS 2012. Then the model applied the predicted probabilities of health transitions and the health status of the new 50/51 year cohorts to the sample of individuals in the MHAS 2012 to calculate the future health status. This process was repeated every two years in the projections until 2050, and then summary variables were calculated.

Since we anticipated that the new cohorts in the future are going to have different characteristics than the current ones, we calculated and applied trends for diabetes prevalence, BMI and smoking status using data on younger cohorts from an alternative source of information, the Mexican National Health and Nutrition Surveys (ENSA 2000 and ENSANUT 2006 and 2012), a series of repeated national cross-sections in Mexico. Based on the observed/predicted characteristics (education, BMI, smoking) of the younger cohorts who will enter ages 50/51 in the future, we anticipate that the future 50/51 year olds will have higher prevalence of diabetes, overweight and obesity, and also higher education than the current 2012 cohort. These results are not shown but are available from the Technical Appendix

The FEM-Mexico simulation is implemented by loading the 50+ MHAS population in 2012, then applying the 2-year transition models for mortality and incidence of health conditions (Diabetes, other Comorbidities, ADL's, IADL's, BMI, and Smoking Status) with Monte Carlo decisions to calculate the new states of the population every two years. The total population is estimated by adjusting for immigration and mortality forecasts using data from the Mexican National Population Council (CONAPO) projections. The new 50/51 year olds are added to the simulation every two years. Finally summary variables are computed.

We simulated four scenarios for the projected diabetes prevalence rates among population 50 and older through 2050. We adopted these scenarios to estimate the potential benefits of prevention programs (18) according to the results from (21) about the efficacy of alternative interventions, for example by changing lifestyle and using prescription drugs: 1) *Status quo*, or no-intervention. This scenario assumes that the current trends will continue, that is, current rates of e.g. smoking, obesity, other diseases, will continue unchanged. 2) 60% reduction in the incidence of diabetes starting at age 50 in 2014, and this is assumed for every cohort entering age 50 in the future. According to the DPP an intensive lifestyle intervention and medication (e.g. metformin) among high-risk cases could reduce the incidence of diabetes by 60%, thus we simulated a scenario under such assumption. 3) 30% reduction in 2-year diabetes incidence, assuming that older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014, and 4) a modest 10% reduction in 2-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and economic policies are

implemented to reduce diabetes risk factors starting at age 50, that is, among the entering cohorts, but the interventions impact the behaviors of all age groups starting in 2014.

The resulting number of diabetes cases for each scenario are used to estimate the consequences of future diabetes in terms of health care resources. To gauge the consequences of future diabetes in terms of health care resources, we obtain a gross estimate of the total number of medical visits that would be used among patients with and without diabetes, and the corresponding total health care cost for medical visits. In the results section, first we present the descriptive characteristics of the 50 years and older population in 2012, the starting period of the simulations. Next, we present the incidence of the health conditions between 2001 and 2003, as well as the marginal effects of the covariates for each one of the equations but with a special focus on the diabetes equation and diabetes as a covariate in other equations. Finally, we present a summary of projected values for a selection of years between 2012 and 2050.

Results

Table 1 presents descriptive statistics. In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico; of these 19.3% had been diagnosed with diabetes, 37.9% with hypertension, and the prevalence for each of the other diseases (heart attack, stroke, lung disease and cancer) was less than 5%. The percentage of the population reporting difficulties to perform at least one of the ADL's and IADL's was 12.8% and 8.9%, respectively, and the percentage of population reporting difficulty in at least one of either ADL's or IADL's was 16.6%. Of the total population aged 50 and older, 35.1% had normal weight, 42.8% were overweight and 22.0% were obese in some degree. The average age was 62.6 years, 46.9% were men and 53.1% women, almost half of the 50 years and older population reported less than basic schooling (0-5 years), and 1 in every 10 had at least some college degree; 70% were married and 15.4% were widowed with important differences by sex.

The 2001-2003 diabetes incidence was 4.3% and the factors significantly associated with the onset of diabetes were: education, hypertension, and BMI. Higher education was associated with lower probability of having a new case of diabetes. However, this likelihood increased by 1.5% for those with hypertension, 0.8% for those living in urban environments, 1.4% for the

overweight and 2.7% for the obese population. As a predictor in the equations for other diseases and health outcomes, diabetes had significant effects, increasing the two-year probability of death by 2.1%, and the two-year incidence of hypertension by 3.2%, of a heart attack by 0.6% and of a stroke by 1.0% (See table 2).

Regarding the results of the four scenarios, Table 3 provides projections for the years 2012, 2020, 2030, 2040 and 2050, of the prevalence of diabetes, the total population, the total number of medical visits per year, the number of diabetics, and the number of cases averted by comparing to the no-intervention scenario. The no-intervention scenario shows that the population 50 years and older is projected to increase from 20.7 million in 2012 to 48.0 million in 2050, and the prevalence of diabetes from 19.3 to 34.0%. Under the scenario of 30% reduction in two-year diabetes incidence, the total population is projected to increase to 48.6 million in 2050 and the prevalence of diabetes will be 28.6%. Both the projected reduction in the prevalence of diabetes (5.4 points) and in mortality (552,000 more individuals) could be attributed to the 30% diabetes incidence reduction. An intermediate and perhaps more plausible scenario is the 10% reduction in two-year diabetes incidence. In this scenario the population in 2050 will be 48.2 million and the prevalence of diabetes will be 32.3%, a 1.7 points reduction of the prevalence when compared with the no-intervention scenario. The 60% diabetes incidence reduction could lead to a 22.8% prevalence of diabetes in 2050 and 49.2 million individuals aged 50 and older.

The average age of death for the population was 75.3 years in 2012. According to the projections of the FEM-Mexico under the no-intervention scenario, the average age at death was 76.7 years in 2050; 76.8 for the scenario of 10% diabetes incidence reduction; 77.0 years for the 30% diabetes incidence reduction scenario, and 77.3 years for the 60% reduction scenario.

We turn now to the economic consequences of diabetes. Since the MHAS has no data available for the average annual cost by disease, we use a rough approximation from two other sources to gauge the difference in cost related to the presence or absence of diabetes. According to the New York State Diabetes Prevention and Control Program, in 2007 the average yearly health care costs for a U.S. person without diabetes is \$2,560 dollars (including institutional care, outpatient care, outpatient medications and supplies); for a person with diabetes that figure

rises to \$11,744 (22). This means that the average cost of a patient with diabetes is 3.5 times greater than for someone without the disease. For Mexico and according to Rodriguez-Bolaños (5), in the Mexican Institute of Social Security (IMSS) the annual cost for a patient with diabetes was \$3,193. We applied the 3.5 times ratio, and obtained that a person without diabetes on average costs \$912 per year.

Based on the average health care costs of the diabetic and non-diabetic population, and the projected population in each group, and assuming that the health care cost ratio among the diabetic and non-diabetic population is going to be constant over the time, we calculated the individual average yearly health care cost for the years 2012 and 2050. For example, in 2012, the total health care cost for the diabetic population was \$12,802 million (4.0 million * \$3,193) and for the non-diabetic population was \$15,247 million (16.7 million * \$912). Adding these two amounts, we calculated \$28,049 million in total health care cost for the total population. The individual average yearly cost for 2012 was \$1,353, obtained by dividing the total health care cost by the total population (\$28,049/20.7 million). If we estimate the average health care cost at the individual level for the year 2050, in the no-intervention scenario the average health care cost would be \$1,663 dollars; in the 10% diabetes incidence reduction scenario, it would be \$1,624 dollars; for the 30% reduction it would be around \$1,544 dollars; and for the 60% reduction the average health care cost per individual would be \$1,416 dollars. If we multiply the individual average health care cost by the total population, the annual savings can be obtained by comparing to the no- intervention scenario, representing \$1,593 million for the 10% diabetes reduction scenario, \$4,849 million for the 30% reduction scenario, and \$10,190 million for the 60% diabetes incidence reduction scenario (See Table 4).

Another aspect of the economic consequences of diabetes is the estimated share of the total national health expenditures that the diabetic population represents. According to the World Health Organization Global Health Expenditure database, the total expenditures in health care in Mexico is about \$28,049 million. Using figures from Table 4, in 2012 the health care cost of the diabetic population represents 45.6% (\$12,802 million /\$28,049 million) of the total health care cost. Similarly, in 2050 due to the increase in the diabetes prevalence and based on the no-intervention scenario, the health care cost of the diabetic population will represent 63.2% of the

total. The equivalent share for the 10% reduction scenario would be 61.4%, compared to 57.3% share under the 30% reduction scenario, and for the 60% diabetes incidence reduction scenario the health care cost of the diabetic population represents 49.8% of the national health care cost.

To supplement the information about the economic consequences of diabetes, we use MHAS data to estimate that, in 2012 the 50 years and older population on average had 4.9 medical visits a year; yet the individuals with diabetes had more medical visits (8.3) compared to the older adults without diabetes (annual average of 4.1). Our microsimulation estimates are that in 2050, under the no-intervention scenario, the average number of medical visits would be 6.4, 8.8 and 5.2 respectively, and the increase in the average number of medical visits is mostly related to the presence of diabetes and other health conditions, for example hypertension.

If we compare the total number of medical visits year by year for the no-intervention scenario *versus* the 10% reduction in two-year diabetes incidence, we cannot find a large difference. However, if we examine the cumulative number of avoided medical visits from 2012 to 2050, the perspective is quite different. In 2012 a medical visit in the Mexican Institute of Social Security (IMSS) costs \$559 pesos (\$35 US dollars) (23). With the projection results, and assuming that this visit cost remains the same in constant terms, we can roughly compare the no-intervention with the 30% incidence diabetes reduction scenario. We calculated 49.2 million avoided medical visits from 2012 through 2050, which represents \$2,047 million dollars in savings. Similarly, we estimate 547,543 avoided medical visits between 2014 and 2016 representing \$10.4 million dollars in savings (data not shown).

Similarly, we estimate the number of cases that could be averted if we could reduce the incidence/prevalence of diabetes. When comparing the no-intervention scenario versus the 30% diabetes incidence reduction scenario (with say, lifestyle modification), we calculated for the year 2020 a total of 816,320 annual averted cases of diabetes, and for the year 2050, 2.5 million. If we compare with the 60% diabetes incidence reduction scenario (with metformin plus lifestyle modifications), the averted cases of diabetes would be 1.6 million in 2020 and 5.4 million in 2050 (see figure 3).

Discussion

In the present study we forecast the diabetes prevalence in Mexico under four scenarios for diabetes incidence reduction: no-intervention, and 10%, 30% and 60% reductions. Our simulation results, from 2012 through 2050, underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions, which drive a significant rise in health care costs. We provide estimates of the impact that a reduction in the diabetes incidence could represent for the public health system in terms of the amount of population without diabetes and the corresponding savings in health care costs.

The analysis of specific diabetes prevention interventions is beyond the scope of our paper, but previous authors have contributed vastly to this body of evidence. Previous research using medical trials has found that interventions to reduce the incidence of diabetes could delay the onset of the disease and reduce its prevalence by 10-60% depending on the duration of the interventions and the strategies used, ranging from lifestyle changes to prescribed drugs, or a combination of both (16,24,25). This body of research suggests that public policies could focus on lifestyle modification, weight loss and increased physical activity to prevent or delay diabetes (25). In addition, these studies highlight the importance of interventions that identify individuals at the highest risk of developing diabetes in order to maximize the effectiveness of interventions and minimize side-effects of interventions with prescribed drugs. For sure, personalized or tailored treatment may not be feasible for the general population, but could represent great gains if applied to certain groups of the population, for example those identified at the highest risk of developing diabetes. Thus, tools to identify those at the highest risk may be highly relevant in countries with limited resources like Mexico. These clinical trials have identified the variety of interventions and heterogeneity of effectiveness, and the upper limit of the scenarios we used in our simulations may be difficult to achieve in clinical practice or at the population level because of the heterogeneity in the characteristics and preferences of the individuals (26). Nevertheless the evidence shows that the interventions intended to delay diabetes could be cost-effective and should be prioritized.

Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in total population with diabetes. These potential

savings represent a rough estimate and may be a lower bound, since we have not considered the benefits of reducing diabetes to the families, and the gains in quality of lives of the individuals involved. Certainly, projections such as the ones we present can serve to raise awareness about major trends with population aging that may affect health, and thus social and economic development (27). The projected scenarios illustrate the future burden of the disease if current trends continue unchanged, as well as the potential beneficial effects if proposed interventions to reduce diabetes prevalence were implemented.

The acceleration of population aging in the coming decades will play a key role in the burden of the disease (4), as older adults are more likely to develop diabetes than younger adults, and mortality among people with diabetes is declining. These two factors, combined with better technology to manage the disease, may increase the prevalence of diabetes and the years spent with the disease. Obesity trends are also important. The current epidemic of obesity in Mexico implies that the health care system needs to quantify the future high cost of the *status-quo*. Our estimates show that if left unchanged, the prevalence of diabetes will reach unprecedented growth by 2050. Thus diabetes is projected to be one of the major challenges for the Mexican aging society, given its prevalence, the associated risk factors, the genetic predisposition of the Mexican population, the high cost of health care and family care for the disease, and in general the economic and health consequences. We hope to have contributed to the knowledge of the potential trends and benefits of possible diabetes prevention and control interventions that can begin now, and that the information provided can prove to be of assistance to decision makers.

Contributors: Cesar Gonzalez Gonzalez (CGG), Bryan Tysinger (BT), Rebeca Wong (RW) and Dana P Goldman (DG) made substantial contributions to the conception and design of the paper. BT assisted with analysis and interpretation of data for this manuscript. CGG analyzed the data, and drafted and revised the paper. RW, BT and DG revised the draft paper critically for important intellectual content. All authors approved of the final version to be published. CGG is the guarantor.

Funding: This study was funded by grants from the National Institute on Aging. The funders had no input into the selection or analysis of data or the content of the final manuscript

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: support from the National Institute of Aging (Grants P30AG024968 and R01AG025533); Dr. Goldman is a founder of Precision Health Economics, a consultancy that provides services to the life sciences industry; and no other relationships or activities that could appear to have influenced the submitted work.

Transparency: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing statement: The MHAS is a public use data set that can be obtained from the MHAS webpage http://www.mhasweb.org/

"I Cesar Gonzalez-Gonzalez The Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs within and any related or stand alone film submitted (the Contribution") has the right to grant on behalf of all authors and does grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licencees, to permit this Contribution (if accepted) to be published in the BMJ and any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence set out at: http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-openaccess-and-permission-reuse."

Please tick **one or more** boxes as appropriate:

I am the sole author of the Contribution.
I am one author signing on behalf of all co-owners of the Contribution.
The Contribution has been made in the course of my employment and I am signing as
authorised by my employer.
I am a US Federal Government employee acting in the course of my employment.
I am not a US Federal Government employee, but some or all of my co-authors are.
I am an employee of the UK Crown* acting in the course of my employment
I am a US Federal Government employee acting in the course of my employment.

□ I am not a US Federal Government employee, but some or all of my co-authors are.
 □ I am an employee of the UK Crown acting in the course of my employment
 □ I am not an employee of the UK Crown acting in the course of my employment but some/all of my co-authors are.*

Bibliography

- 1. OECD. Cardiovascular Disease and Diabetes: Policies for Better Health and Quality of Care. 2015.
- 2. Arredondo A, De Icaza E. Costos de la Diabetes en América Latina: Evidencias del Caso Mexicano. Value Heal. 2011;14(5 SUPPL.):S85–8.
- 3. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, et al. Ensanut 2012Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. [Internet]. Instituto Nacional de Salud Pública. Cuernavaca; 2012. Available from: http://ensanut.insp.mx/informes/ENSANUT2012ResultadosNacionales.pdf
- 4. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr. 2010;8(1):29.
- 5. Rodríguez Bolaños R, Reynales Shigematsu LM, Jimenez Ruiz JA, Juárez Márquez SA, Hernández Ávila M. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2010;28(6):412–20.
- 6. OECD. Projecting OECD Health and Long-Term Care Expenditures: What Are the Main Drivers? 2006.
- 7. Rull J a., Aguilar-Salinas C a., Rojas R, Rios-Torres JM, Gómez-Pérez FJ, Olaiz G. Epidemiology of type 2 diabetes in Mexico. Arch Med Res. 2005;36(3):188–96.
- 8. IDF. Diabetes Atlas. Seventh Edition. 2015.
- 9. Mata M, Antoñanzas F, Tafalla M, Sanz P. El coste de la diabetes tipo 2 en España. Gac Sanit. 2002;16(6):511–20.
- 10. Bertram MY, Lim SS, Barendregt JJ, Vos T. Assessing the cost-effectiveness of drug and lifestyle intervention following opportunistic screening for pre-diabetes in primary care. Diabetologia. 2010;53(5):875–81.
- 11. Pinto G, Beltrán-sánchez H. Prospective study of the link between overweight / obesity and diabetes incidence among Mexican older adults: 2001-2012. Salud Publica Mex. 2015;57(1):s15–21.
- 12. Rtveladze K, Marsh T, Barquera S, Sanchez Romero LM, Levy D, Melendez G, et al. Obesity prevalence in Mexico: impact on health and economic burden. Public Health Nutr. 2014;17(1):233–9.
- 13. Wolf DA. Synthetic Trajectories obtained by matching longitudinal data. 2014.
- 14. Zucchelli E, Jones A, Rice N. The evaluation of health policies through dynamic

- microsimulation methods. UK; 2012.
- 15. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: A systematic review. Diabetes Care. 2010;33(8):1872–94.
- 16. Knowler W, Barret-Connor E, Fowler S, Hamman R, Lachin J, Walker E, et al. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. N Engl J Med [Internet]. 2002 Feb 7;346(6):393–403. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa012512
- 17. Goldman DP, Zheng Y, Girosi F, Michaud PC, Olshansky SJ, Cutler D, et al. The benefits of risk factor prevention in Americans aged 51 years and older. Am J Public Health. 2009;99(11):2096–101.
- 18. Olshansky SJ, Goldman DP, Zheng Y, Rowe JW. Aging in America in the Twenty-First Century: Demographic Forecasts from the MacArthur Foundation Research Network on an Aging Society Published by: Wiley on behalf of Milbank Memorial Fund content in a trusted digital archive. We use information techn. Milbank Q. 2013;87(4):842–62.
- 19. Goldman DP, Lakdawalla D, Michaud P, Eibner C, Zheng Y, Gailey A, et al. The Future Elderly Model: Technical Documentation. 2015.
- Wong R, Michaels-Obregon A, Palloni A. Cohort Profile: The Mexican Health and Aging Study (MHAS). Int J Epidemiol. 2015;1–10.
- 21. Gregg EW, Boyle JP, Thompson TJ, Barker LE, Albright AL, Williamson DF. Modeling the impact of prevention policies on future diabetes prevalence in the United States: 2010-2030. Popul Health Metr. 2013;11(1):18.
- 22. Ayatollahi H, Hasannezhad M, Fard HS, Haghighi MK. Type 1 diabetes self-management: developing a web-based telemedicine application. Heal Inf Manag J. 2015;1–12.
- 23. Rodríguez Bolaños RDLÁ, Reynales Shigematsu LM, Jiménez Ruíz JA, Juárez Márquezy SA, Hernández Ávila M. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2012;28(6):412–20.
- 24. Tuomilehto J, Lindstrom J, Eriksson J, Valle T, Hamailanen H, Ilanne-Parikka P, et al. Prevention of Type 2 Diabetes Mellitus By Changes in Lifestyle Among Subjects With Impaired Glucose Tolerance. N Engl J Med. 2001;344(18):1343–50.
- 25. Guthrie DW. The Prevention or Delay of Type 2 Diabetes. Clin Diabetes [Internet]. 2002 Jul 1;20(3):109–16. Available from: http://care.diabetesjournals.org/cgi/doi/10.2337/dc15-S008
- 26. Dorresteijn JAN, Visseren FLJ, Ridker PM, Wassink AMJ, Paynter NP, Steyerberg EW, et al. Estimating treatment effects for individual patients based on the results of randomised clinical trials. BMJ [Internet]. 2011;343:d5888. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3184644&tool=pmcentrez&re ndertype=abstract
- 27. Imhoff E van, Post W. Microsimulation Methods for Population Projection. Popul An

English Sel. 2008;10(1):97–138.

Table 1. Characteristics of the population 50 years and older, MHAS 2012

	%	
Age (mean)	62.6	
Sex (male)	46.9	
Education		
Less than complete basic (0 to 5 years)	46.4	
Basic complete (6 years)	20.8	
High school (7 to 12 years)	22.8	
College (13+ years)	10.0	
Marital Status		
Single	5.1	
Married	69.8	
Separated/Divorced	9.6	
Widowed	15.5	
Chronic diseases (% Yes)		
Hypertension	37.9	
Diabetes	19.4	
Cancer	1.2	
Heart attack	3.0	
Lung disease	5.1	
Stroke	2.2	
Disability (%)		
Any ADL (1+)	12.9	
Any IADL (1+)	11.7	
Any ADL or Any IADL	19.3	
Body Mass Index (BMI)		
Normal (< 25.00 kg/m ²)	35.1	
Overweight (25.00 to 29.99 kg/m²)	42.9	
Obese 1 (30.00 to 34.99 kg/m²)	16.7	
Obese 2 (35.00 to 39.99 kg/m²)	3.8	
Obese 3 (≥40 kg/m²)	1.6	
Smoking Status		
Never	63.7	
Former	23.4	
Current	13.0	

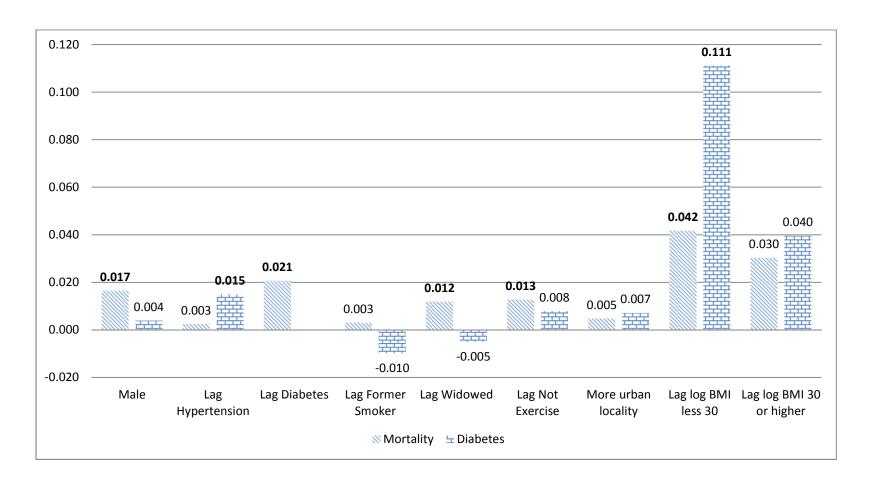
Source: MHAS 2012. Weighted statistics.



Table 2: Incidence equations for mortality, chronic diseases, smoking status and BMI for the population 50 years and older, FEM-Mexico 2001-2003 (Marginal effects)

				Heart		Lung		Smoke	Log
	Mortality	Diabetes	Hypertension	attack	Cancer	Disease	Stroke	(Current)	BMI
TWO YEAR INCIDENCE	2.3	4.3	16.1	1.4	0.4	2.7	0.5	8.5	3.3
	Marginal effects								
Lag age 50-64	0.002	-0.001	0.003	0.001	0.000	0.001	0.000	-0.003	0.002
Lag age 65-74	0.001	-0.002	-0.002	0.001	0.000	0.000	0.001	-0.001	-0.004
Lag age 75+	0.003	0.000	-0.001	0.000	-0.001	0.001	0.000	-0.004	0.000
Male	0.017	0.004	-0.049	0.004	0.000	-0.001	-0.001	0.124	-0.004
Basic school	0.005	0.021	-0.039	-0.009	0.005	-0.014		-0.023	0.028
Highschool	0.012	-0.030	-0.005	-0.002	0.006	-0.007	0.005	0.015	0.005
College	-0.013	-0.019	-0.042	0.005	0.006	-0.012	-0.003	0.011	0.012
Lag Hypertension	0.003	0.015		0.016			0.004	-0.036	0.007
Lag Diabetes	0.021		0.034	0.007			0.010	-0.019	-0.003
Lag Heart attack	0.017						0.002	-0.021	0.013
Lag Cancer	0.074						-0.002	-0.010	-0.001
Lag Lung Disease	0.011							0.005	-0.003
Lag Stroke	0.027							-0.025	0.001
Lag 1 IADL	0.001							-0.019	-0.001
Lag 2+ IADL	0.000							-0.036	-0.014
Lag 1 ADL	0.013							0.014	0.001
Lag 2 ADL	0.057							0.035	0.008
Lag 3+ ADL	0.154							0.038	0.014
Lag Former smoker	0.003	-0.010		0.003	0.002	-0.002	0.003		0.002
Lag Widowed	0.012	-0.005		-0.001	-0.002	0.002	-0.001	0.014	0.000
Lag NOT Exercise	0.013	0.008	0.020	0.007	0.001	0.006	0.002	0.120	0.010
More urban locality	0.005	0.007	-0.008	-0.003	0.001	-0.010	0.001	0.014	0.017
Lag BMI less than 30	0.042	0.111	0.114	0.008					0.968
Lag BMI 30 or higher	0.030	0.040	0.186	-0.008					0.616

Figure 1: Marginal effects for Mortality and Diabetes Equations, FEM-Mexico, 2001-2003



NOTE: See table 2 for full regression results

Table 3: Projection of prevalence of diabetes, total population and number of medical visits by Simulation Scenarios, Population 50 years and older, FEM-Mexico simulation 2012-2050

ESTIMATE by SCENARIO	2000	2006	2012	2020	2030	2040	2050
Diabetes prevalence (%)							
Observed	12.00	15.74	19.34				
No intervention			19.34	26.24	30.69	32.91	34.00
10% incidence reduction			19.34	25.23	29.29	31.29	32.25
30% incidence reduction			19.34	23.32	26.27	27.74	28.64
60% incidence reduction			19.34	20.42	21.35	22.05	22.76
Total Population							
No intervention			20,727,415	26,781,877	34,641,639	41,652,429	48,010,723
10% incidence reduction			20,727,415	26,794,525	34,705,941	41,774,461	48,180,921
30% incidence reduction			20,727,415	26,814,809	34,832,223	42,027,492	48,563,485
60% incidence reduction			20,727,415	26,851,575	35,021,745	42,468,762	49,191,108
Number of medical visits (A	nnual)						
No intervention			102,183,113	151,881,059	216,505,084	274,138,503	324,866,875
10% incidence reduction			102,183,113	151,328,257	215,568,988	273,165,155	323,819,400
30% incidence reduction			102,183,113	150,258,034	213,441,667	270,708,771	321,751,070
60% incidence reduction			102,183,113	148,650,611	209,909,778	267,031,679	318,180,682
Number of diabetics (Annua	I)						
No intervention			4,009,290	7,364,738	11,155,124	14,407,673	17,209,864
10% incidence reduction			4,009,290	7,083,003	10,660,831	13,737,582	16,380,310
30% incidence reduction			4,009,290	6,548,418	9,587,597	12,240,966	14,648,013
60% incidence reduction			4,009,290	5,736,938	7,826,970	9,816,176	11,773,857
Averted cases of diabetes							
(vs. no-intervention)				004 705	404.000	070 000	000 55
10% incidence reduction			-	281,735	494,293	670,092	829,554
30% incidence reduction			-	816,320	1,567,527	2,166,708	2,561,851
60% incidence reduction			-	1,627,799	3,328,153	4,591,497	5,436,007

Figure 2: Diabetes Prevalence for Scenarios of Diabetes Incidence Reduction, Population aged 50 and older.FEM-Mexico 2012-2050

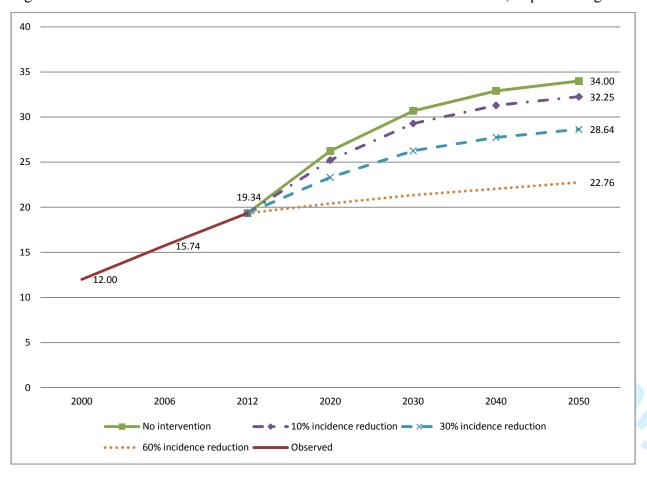
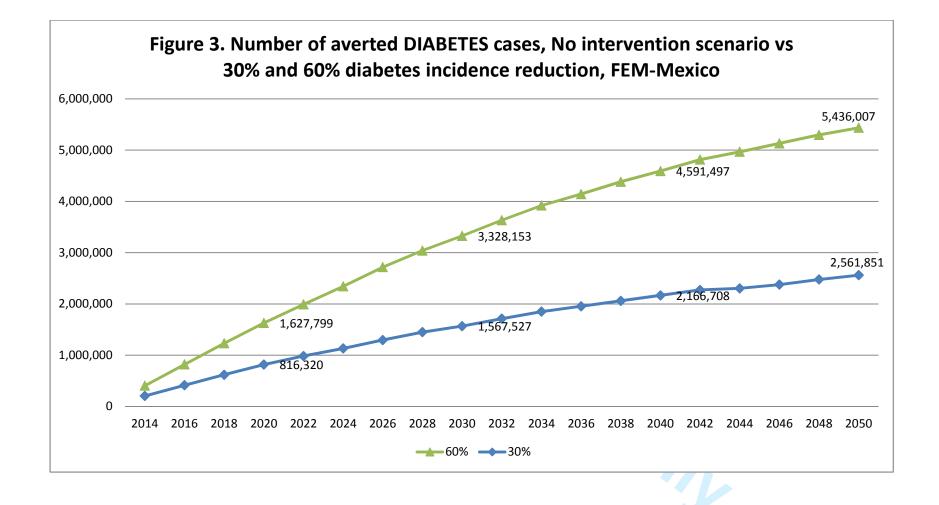


Table 4: Projection of total population, percentage, and health care cost by diabetes status, Population aged 50 and older. FEM-Mexico simulation 2012-2050

Chavastavistica	2012	2050					
Characteristics	2012	No intervention	10% reduction	30% reduction	60% reduction		
Total Population	20,727,415	48,010,723	48,180,921	48,563,485	49,191,108		
Proportion of population by Diabetes diagnosis							
With	19.34	34.00	32.25	28.64	22.76		
Without	80.66	66.00	67.75	71.36	77.24		
Total Population by Diabetes Condition							
With	4,009,290	15,797,928	15,031,288	13,451,263	10,858,373		
Without	16,718,125	32,212,795	33,149,633	35,112,222	38,332,735		
Total Health care costs by diabetes condition							
With	12,801,662,970	50,442,784,104	47,994,902,584	42,949,882,759	34,670,784,989		
Without	15,246,930,000	29,378,069,040	30,232,465,296	32,022,346,464	34,959,454,320		
Total	28,048,592,970	79,820,853,144	78,227,367,880	74,972,229,223	69,630,239,309		
Individual average Health care cost	1,353	1,663	1,624	1,544	1,416		



Modeling Diabetes and Related Medical Care of the Future Elderly in Mexico

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

Technical Appendix

Structure of the microsimulation model

The structure of the FEM-Mexico microsimulation and the differences with the HRS-FEM are presented in the Appendix Figure 1. Our simulation starts in 2012 with 20.7 Million individuals age 50+ (17.7% of the population in 2012; (CONAPO, 2012)). The simulation model estimates the risk of developing diabetes, other five chronic diseases and the survival status for each individual. Due to the structure of the model, every two years the microsimulation model updates the health status and mortality risk for each individual. To replenish the youngest cohorts, a new cohort of 50 and 51 year-old individuals are added at the beginning of each simulated cycle.

This technical appendix describes only the adaptations made to the FEM in order to work with the Mexican Health and Aging Study (MHAS), in depth details of the FEM are published everywhere (add reference).

The model's main variables are age, gender, smoke, BMI and six chronic conditions (hypertension, diabetes, heart disease, lung disease, stroke and cancer). We also create an indicator variable mortality. The baseline cohort is defined at the initial period (2001). This time period represents the first two years of the simulations (i.e.,2012 and 2013). The variables age, gender, smoke, BMI and chronic conditions are sampled from MHAS with replacement. These samples are repeated until the number of individuals in each age and sex category are equal to the Mexican population distribution in 2012.

After establishing the baseline cohort, the microsimulation iterates to the next time period by projecting the values of each variable for the next two years (i.e., 2014 and 2015). Since the 50 and 51 years individuals age to 52 and 53 years-old, respectively, at time 2, new 50 and 51 year-old individuals are added to the simulation to replenish the youngest age group. The characteristics of these new individuals are sampled with replacement from the 50-51 year-old individuals in MHAS 2012, weighted by the age- and gender-specific projected population of 50 year-olds based on the official Mexican projections (CONAPO) and imposing the trends for some of the main variables.

MHAS provides self-reported chronic conditions for each individual in 2001, 2003 and 2012. We use logistic regressions to estimate the probability of transitioning to one of the six mutually exclusive health states in 2003 based on not having that chronic condition in 2001, controlling for demographic and comorbid conditions in 2001. Then we projected transitions of self-reported diabetes, hypertension, heart attack, cancer, stroke and lung disease. The independent variables

include health status measures and basic demographic characteristics such as age, gender, smoking status or weight category, as measured at baseline in 2001. The coefficient estimates of these transitions models predict health status two years into the future (2003). All chronic conditions are treated as absorbing states.

Specific situations for FEM-Mexico

a. Inter-wave gap period

The first difference between the structure of the FEM-Mexico and the FEM was that in the latter, the main source of information, the Health and Retirement Study (HRS), is collected every two years and the microsimulation uses this gap time to estimate health status of the individuals. In MHAS there is three available waves, 2001, 2003 and 2012 with different inter-wave periods. We had to choose our baseline population based on the advantages that the microsimulation model presents and we decided to use the 2012 data as a baseline and the 2001-2003 information to estimate the health transitions and to run our microsimulation.

b. Cross-validation: Cohort analysis (MHAS 2003-2011/2013)

The next step was to corroborate that adapting the MHAS information to the FEM could lead to acceptable forecast of diabetes, to do so we run a cohort analysis using wave 2 (2003) as the start point of the simulation, then we compare the results obtained from the FEM-Mexico with the real data from MHAS wave 3 (2012). Results show that FEM-Mexico predicts effectively the prevalence of diabetes (see figure 2).

- c. Demographic adjustments to run the simulation
- 1) Since age and sex distribution in the MHAS differs from the CONAPO projections we reweight the population by age and sex to have a common start point for the projections (see Figure 3).
- 2) Using the CONAPO projections (2010-2050) we made some adjustments on mortality probabilities and due to evident differences by age group we adjust for two groups: 50 to 64 years and 65 years and older, all calculations relative to 2012 level (see table 1)
- 3) Migration adjustments [by year (2013-2050) single age and sex], all calculations relative to 2012 level.
 - d. Incoming cohorts (new 50-51 years old)

We assume that the new 50-51 years old individuals will be different in several characteristics. For example, with respect to the actual cohorts, they will be more educated, with lower tobacco and alcohol consumption and with higher BMI. Using information from the Mexican National

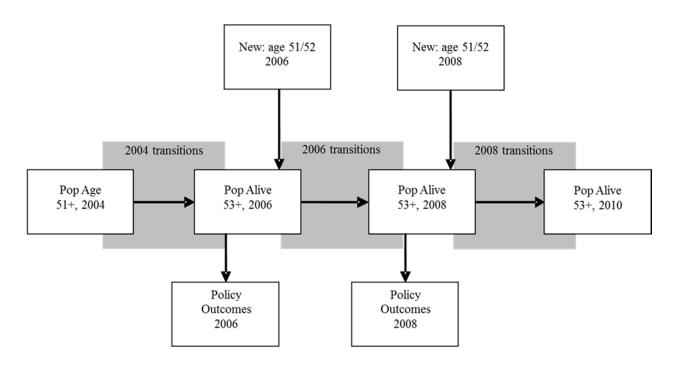
Health Surveys (2000, 2006 and 2012) we predicted trends for these variables and applied them to the incoming cohorts (50-51 years old).

e. Missing data.

We used records in which the information for all the variables is complete.



Figure 1. **Architecture of the FEM**



HRS-FEM and FEM-Mexico differences

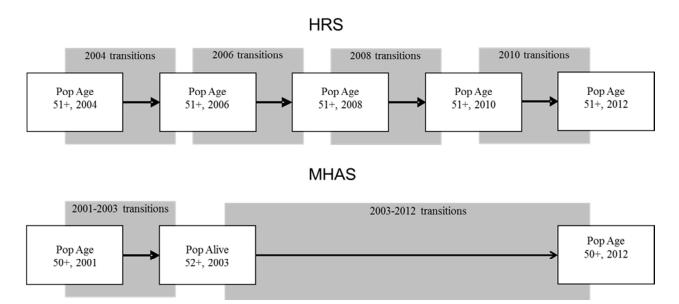
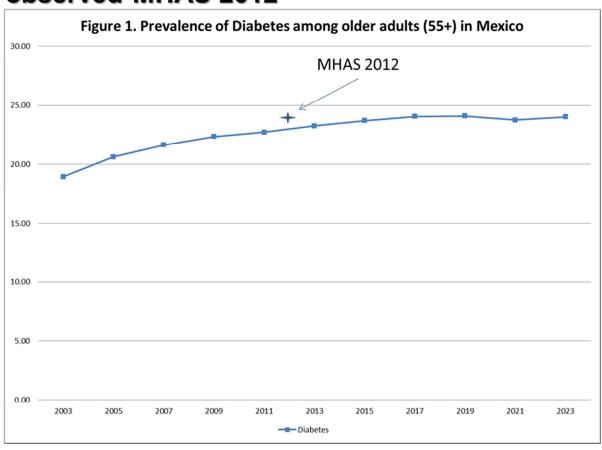


Figure 2.

Comparison between microsimulation and observed MHAS 2012



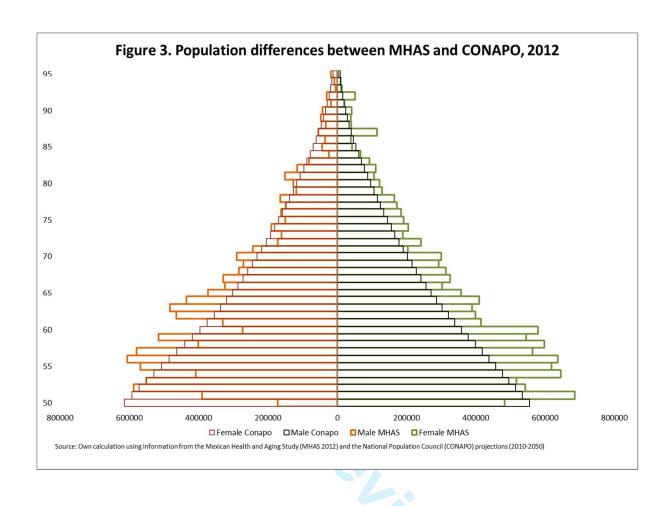


Table 1. Trends for mortality, diabetes, Body Mass Index and Smoking, 2012-2050

Year	Mortality	adjustments ¹	Diabetes ²		Body Mass Index ²				king ²
Teal	50-64	65+	Diabetes	Overweight	Obese 1	Obese 2	Obese 3	Current	Former
2012	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
2013	0.9920	0.9983	1.0176	1.0007	1.0119	1.0196	1.0458	1.0309	0.9856
2014	0.9838	0.9962	1.0354	1.0014	1.0239	1.0396	1.0935	1.0624	0.9714
2015	0.9756	0.9934	1.0534	1.0020	1.0359	1.0599	1.1433	1.0947	0.9573
2016	0.9671	0.9901	1.0718	1.0027	1.0480	1.0806	1.1952	1.1277	0.9434
2017	0.9585	0.9861	1.0904	1.0034	1.0602	1.1015	1.2492	1.1614	0.9296
2018	0.9498	0.9817	1.1092	1.0041	1.0725	1.1229	1.3056	1.1959	0.9160
2019	0.9407	0.9769	1.1283	1.0048	1.0848	1.1445	1.3642	1.2310	0.9026
2020	0.9317	0.9718	1.1477	1.0055	1.0971	1.1665	1.4253	1.2669	0.8892
2021	0.9227	0.9666	1.1674	1.0061	1.1096	1.1889	1.4888	1.3035	0.8761
2022	0.9138	0.9614	1.1873	1.0068	1.1220	1.2116	1.5549	1.3408	0.8630
2023	0.9051	0.9563	1.2075	1.0075	1.1346	1.2347	1.6237	1.3788	0.8502
2024	0.8965	0.9515	1.2279	1.0082	1.1472	1.2581	1.6952	1.4175	0.8374
2025	0.8882	0.9470	1.2487	1.0089	1.1598	1.2819	1.7695	1.4569	0.8249
2026	0.8802	0.9428	1.2697	1.0096	1.1725	1.3061	1.8467	1.4969	0.8124
2027	0.8722	0.9388	1.2909	1.0103	1.1852	1.3306	1.9268	1.5377	0.8002
2028	0.8641	0.9351	1.3125	1.0109	1.1980	1.3555	2.0100	1.5791	0.7880
2029	0.8561	0.9316	1.3343	1.0116	1.2109	1.3807	2.0964	1.6212	0.7760
2030	0.8480	0.9282	1.3564	1.0123	1.2238	1.4064	2.1859	1.6640	0.7642
2031	0.8400	0.9251	1.3788	1.0130	1.2367	1.4324	2.2787	1.7074	0.7525
2032	0.8319	0.9221	1.4014	1.0137	1.2497	1.4588	2.3749	1.7514	0.7409
2033	0.8236	0.9195	1.4244	1.0144	1.2627	1.4855	2.4744	1.7960	0.7295
2034	0.8149	0.9172	1.4476	1.0150	1.2757	1.5126	2.5775	1.8412	0.7182
2035	0.8058	0.9153	1.4711	1.0157	1.2888	1.5402	2.6841	1.8870	0.7071
2036	0.7962	0.9138	1.4949	1.0164	1.3019	1.5681	2.7943	1.9334	0.6961
2037	0.7866	0.9128	1.5189	1.0171	1.3150	1.5963	2.9082	1.9803	0.6852
2038	0.7766	0.9124	1.5432	1.0178	1.3282	1.6250	3.0259	2.0277	0.6745
2039	0.7660	0.9125	1.5678	1.0185	1.3414	1.6540	3.1472	2.0757	0.6639
2040	0.7551	0.9133	1.5927	1.0192	1.3546	1.6835	3.2724	2.1241	0.6535
2041	0.7439	0.9146	1.6179	1.0198	1.3678	1.7133	3.4015	2.1730	0.6431
2042	0.7327	0.9163	1.6433	1.0205	1.3811	1.7434	3.5344	2.2223	0.6330
2043	0.7216	0.9183	1.6690	1.0212	1.3944	1.7740	3.6712	2.2721	0.6229
2044	0.7106	0.9206	1.6950	1.0219	1.4077	1.8050	3.8119	2.3222	0.6130
2045	0.6997	0.9234	1.7213	1.0226	1.4210	1.8363	3.9565	2.3727	0.6032
2046	0.6892	0.9267	1.7478	1.0233	1.4343	1.8680	4.1050	2.4235	0.5936
2047	0.6791	0.9303	1.7746	1.0239	1.4477	1.9001	4.2574	2.4747	0.5841
2048	0.6694	0.9340	1.8017	1.0246	1.4610	1.9326	4.4136	2.5261	0.5747
2049	0.6600	0.9376	1.8290	1.0253	1.4744	1.9655	4.5737	2.5778	0.5654
2050	0.6517	0.9419	1.8566	1.0260	1.4877	1.9987	4.7376	2.6297	0.5563

¹ Trends calculated using CONAPO Projections (2010-2050)

² Trends calculated using Mexican National Health Surveys (2000, 2006 and 2012)

BMJ Open

Projecting diabetes among older adults in Mexico: The Future Elderly Model-Mexico (FEM-Mexico)

Journal:	BMJ Open
Manuscript ID	bmjopen-2017-017330.R1
Article Type:	Research
Date Submitted by the Author:	28-Jul-2017
Complete List of Authors:	Gonzalez Gonzalez, Cesar; Universidad de Colima, Facultad de Trabajo Social Tysinger, Bryan; University of Southern California Goldman, Dana; University of Southern California Wong, Rebeca; University of Texas, Department of Preventive Medicine and Community Health
Primary Subject Heading :	Diabetes and endocrinology
Secondary Subject Heading:	Public health, Health economics
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, HEALTH ECONOMICS, PUBLIC HEALTH

SCHOLARONE™ Manuscripts

Projecting diabetes among older adults in Mexico: The Future Elderly Model-Mexico (FEM-Mexico)

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

School of Social Work, University of Colima, Mexico, Cesar Gonzalez-Gonzalez professor Roybal Center for Health Policy Simulation, University of Southern California, Bryan Tysinger director

Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Dana P Goldman director,

Sealy Center on Aging, University of Texas Medical Branch, Rebeca Wong professor

Corresponding author: C Gonzalez-Gonzalez cgonzalez31@ucol.mx

Abstract

Objective Diabetes has been growing as a major health problem and a significant burden on the population and on health systems of developing countries like Mexico that are also aging fast. The goal of the study was to estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes.

Design A simulation study using longitudinal data from three waves (2001, 2003 and 2012) of the Mexican Health and Aging Study (MHAS) and adapting the Future Elderly Model (FEM) to simulate four scenarios of hypothetical interventions that would reduce diabetes incidence, and to project the future diabetes prevalence rates among populations 50 years and older.

Participants Data from 14,662 participants with information on self-reported diabetes, demographic characteristics, health and mortality.

Outcome measures We obtained, for each scenario of diabetes incidence reduction, the following summary measures for the population aged 50 and older from 2012-2050: prevalence of diabetes, total population with diabetes, number of medical visits.

Results In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico; 19.3% had been diagnosed with diabetes; and the 2001-2003 diabetes incidence was 4.3%. The no-intervention scenario shows that the prevalence of diabetes is projected to increase from 19.3% in 2012 to 34.0% in 2050. Under the 30% incidence reduction scenario, the prevalence of diabetes will be 28.6% in 2050. Comparing the no-intervention scenario with the 30% and 60% diabetes incidence reduction scenarios, we estimate a total of 816,320 and 1.6 million annual averted cases of diabetes, respectively, for the year 2020.

Discussion Our study underscores the importance of diabetes as a disease by itself, but also the potential health care demands and social burden of this disease and the need for policy interventions to reduce diabetes prevalence.

Strengths and limitations of this study

- The study is the first in Mexico using national representative longitudinal-individual data to project the prevalence of diabetes among older adults in Mexico.
- The study uses an adapted version of the Future Elderly Model, a demographic and economic simulation model designed to project the future costs and health status of the elderly based on their recent past and current health status and taking into account a broad set of risk factors.
- Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes.
- The limitations are related to the nature of the data from the Mexican Health and Aging Study, since the analysis is based on self-reported data and maybe underestimate the prevalence of diabetes. The Future Elderly Model is using only two waves of information to estimate the disease transitions, and this could have an impact on the reliability of results.

Introduction

Diabetes represents a major health problem and a significant burden on health care systems and societies overall. This is particularly the case in countries like Mexico, where the prevalence of diabetes among the population 20-79 years old was 15.9% in 2011. This was the highest in the OECD (1) and ranked No. 9 worldwide (2). According to the national estimates in Mexico, the self-reported prevalence of diabetes among the population aged 60 and older was 24% in 2012, and in the period between 2000 and 2012 the prevalence doubled among those aged 70 and older from 10% to 20%, and among those aged 60-69 the prevalence grew 1.5 times, going from 18% to 26% (3).

Population aging and the growing prevalence of diabetes raise concerns about the increased burden on social, health and family systems because of the known consequences of this disease. People with diabetes may experience additional health complications (4) (5), greater social needs (6), loss in productivity and earnings (7) and diminished quality of life (8) (9). Moreover, in 2012, diabetes was the leading cause of mortality in the Mexican adult population, accounting for 17% of all deaths (10). It is also the leading cause of premature withdrawal from economic activity, blindness and renal failure (11). Diabetes has a direct impact not only on overall life expectancy but also on the quality of life of the older adult population.

A key risk factor associated with diabetes is high body weight (12), as obese or overweight individuals are more likely to become diabetic (13). Estimates from the 2012 National Health Survey in Mexico reveal that 41% of adults aged 30-49 were overweight, 37% obese and 79% had abdominal obesity (14); figures are similar for those aged 50 years and older (3). Furthermore, obesity is projected to increase across all age groups, with serious implications for diabetes patients and for the Mexican health care system (2).

From a public policy perspective, it is important to take a glance into the future burdens and understand how the prevalence of diabetes will change over the next decades. Moreover, since there are health interventions that have proven to be effective in reducing the onset and management of the disease, it is important to understand how current and potential new policies, particularly those designed to prevent or ameliorate the rise of chronic diseases, may alter the

diabetes trends. For sure, the future prevalence of diabetes will be influenced by the momentum of population aging, the trends in obesity and the patterns of medical advances, among other factors. Thus, we estimate the future cases of diabetes among older adults in Mexico, assuming the current patterns of risk factors and behaviors, as well as the likely trends if hypothetical preventive interventions are adopted to reduce the onset of new cases.

One way to assess the future burden of the disease is to use microsimulation models. Projecting the prevalence of diabetes, the number of diabetics in the population and the consequences for the health care system in terms of health care needs can be useful for public health policy makers, in order to raise awareness of the potential consequences of varying paths that the burden of diseases can take, and possibly designate resources to prevent cases. Microsimulation has been used as a tool for social science research and policy analysis (15), and can be used to evaluate the impact of interventions under alternative scenarios (16). Such scenarios often rely on information from clinical trials where evidence strongly supports the ability to prevent or delay the onset of a disease. For example, a systematic review of the literature concludes that a variety of interventions can help reduce the onset and improve the management of diabetes in a diversity of country settings. This review takes into account the costs involved as well (17). Specifically for the United States, the Diabetes Prevention Program (DPP) was a multicenter randomized clinical trial that demonstrated that weight loss through dietary changes and more physical activity could prevent or delay onset of Type 2 diabetes, resulting in 58% reduction in the incidence of diabetes. The DPP also showed that use of a generic oral diabetes drug (metformin) reduced the incidence of disease among at-risk individuals by 31%. Thus, for the purposes of this paper, we consider the future prevalence of diabetes if it were possible to adopt hypothetical public health interventions that reduced the incidence of diabetes on a scale up to the results shown by the DPP (18). We selected these results for simulation of the scenarios, with the caveat that these results might not perfectly apply to Mexico. We are assuming average effectiveness of national-level interventions, which may be difficult to achieve, but the assumed scenarios can help policy makers understand the impact on the burden of diabetes if these various levels of prevention could be achieved, including the projected burden should no intervention be adopted.

The goal of the study was to estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes. We estimate future levels of diabetes under different scenarios for the population aged 50 years and older in Mexico. Were hypothetical interventions to be implemented to reduce the incidence of diabetes, how much would the prevalence of diabetes change? And how would the health care burden of diabetes diminish, in terms of medical resources to treat the disease? To address these questions, we modeled the trajectory of future diabetes in Mexico from 2012 to 2050 using a microsimulation model, the Future Elderly Model (FEM). We construct four scenarios for the projections, estimating the effect of reducing two-year diabetes incidence rates by 0%, 10%, 30% and 60%. We selected the scenarios based on evidence from clinical trials, with effects from as large as that in the clinical trial setting to more attenuated. The microsimulation model takes into account the current prevalence, the estimated new cases of diabetes (incidence) among those aged 50 and older in each two-year period, the deaths among the group 50 and older in each two-year period, and the prevalence among the new population entering the group 50 and older in each two-year period in the future.

Using information on what can be achieved by implementing proven interventions helps us to construct different scenarios that reflect realistic results of adopting these interventions. Combining results from clinical trials, past trends based on national health surveys and individual characteristics from the MHAS could lead to stronger conclusions about the future of diabetes in Mexico.

Methods and data

The FEM is a demographic and economic simulation model, originally designed to project the future costs and health status of the elderly based on their current health status and taking into account a broad set of risk factors (19). In contrast to projection models that use aggregate measures of health traits for a population cohort, the FEM uses information on how individual health characteristics change at the individual level using longitudinal survey data (20). Details on the FEM have been described elsewhere (21).

The individual level data comes from the Mexican Health and Aging Study (MHAS), a prospective survey of a nationally and urban–rural representative sample of adults aged 50 years and older residing in Mexico in 2001 (22). From its inception, the MHAS was designed to be highly comparable to the U.S. Health and Retirement Study (HRS). The MHAS content includes health in multiple domains, health behaviors and risk factors, socioeconomic conditions, work history, health insurance, health expenditures and family background, among others. A next-of-kin module gathers information on deceased study participants. We used three waves of available data: 2001, 2003 and 2012. A refresher sample of individuals aged 50-61 was added in 2012, to once again represent the population aged 50 and older in 2012.

For our purposes, FEM-Mexico uses two main modules of the FEM developed for the U.S. (FEM-US). The first produces individual trajectories, that is, 2 year transitions, and estimates incidence for a number of health conditions and disability statuses. The second module ensures that the data remains representative of the population aged 50 years and older into the future by replenishing the sample, with 50-51 year olds incorporated into the sample every two years.

The data used for the FEM-US and the FEM-Mexico differ in one important methodological aspect, the inter-wave periods. As mentioned above, the FEM was created to be used with the U.S. Health and Retirement Study (HRS), a longitudinal survey collected every two years; MHAS has a two-year gap between the first (2001) and second (2003) wave, and a 9-year gap between the second and third (2012) wave. To overcome this methodological difference, we use the MHAS 2001 and 2003 waves to estimate health transitions and two-year incidence, and we use the 2012 wave as the baseline to start the microsimulation. In other words, we imposed the 2001-2003 health transitions onto the 2012 MHAS population. We tested the adequacy of this approach by applying the 2001 prevalence and the 2001/2003 incidence to project the prevalence of diabetes in 2012. We then compared the estimated prevalence with the prevalence observed in MHAS 2012 and the estimates were quite similar; hence, we concluded that this approach is reasonable. These results are not shown but are provided in the Technical Appendix.

To measure diabetes prevalence, MHAS respondents were asked: "Has a doctor or medical personnel ever told you that you have diabetes or a high blood sugar level?" The equation for the 2001 to 2003 diabetes incidence was used to estimate the probability of developing diabetes, using a probit regression model with covariates measured in 2001 as follows: age (50-64, 65-74, 75+ years), gender (male, female), education (less than basic, basic, high school and college), marital status (single, married, separated/divorced, widowed), ever hypertension (yes, no), body mass index (BMI underweight/normal, overweight, obese¹), smoking status (never, current, or former), physical activity in the last two years (yes, no), size of locality of residence (less than 100,000 inhabitants, 100,000 or more inhabitants) and health insurance (yes, no). To estimate the incidence equation, only the cases that reported no diabetes in 2001 are included in the analytical sample.

We estimated similar incidence equations using probit regression models for self-reported hypertension heart attack, lung disease, stroke and mortality; ordered probit models for smoking status (never, current, former), limitations with five Activities of Daily Living (ADL's) (none, one, two, three or more) and four Instrumental Activities of Daily Living (IADL's) (none, one, two or more) and linear regression models for log (BMI). The list of variables included in the right-hand-side of each equation varies depending on the theoretical relationship of the independent variables with the corresponding dependent variable.

Since FEM works as a simultaneous equations model, the parameters in one equation affect the parameters of the other equations, meaning that transitions could occur in multiple diseases in any given year of the projection. Thus, an individual could have more than one disease transition in the same year, e.g., new diabetes and new hypertension. Similar to FEM-US, in FEM-Mexico, once a health condition (chronic disease) is acquired or mortality occurs, these states are treated as absorbing or permanent.

In addition, we assessed the health-care consequences of diabetes by comparing in each one of the scenarios the number of medical visits by diabetics *versus* non-diabetics. We estimated an OLS equation for the number of medical visits as a dependent variable, including

¹ Underweight/normal is defined as a BMI lower than 25, overweight is defined as a BMI between 25.0 and 29.9 and a BMI of 30 or higher is considered obese.

with/without diabetes as the main explanatory variable. MHAS respondents were asked: "In the last year, how often have you visited or consulted a doctor or medical personnel?"

To maintain representativeness of the 50 year and older population, the microsimulation model needed replenishment cohorts every two years. To replenish the sample, we took the sample of 50/51 year olds that were added to the sample from MHAS 2012. Then, the model applied the predicted probabilities of health transitions and the health status of the new 50/51 year cohorts to the sample of individuals in the MHAS 2012 to calculate the future health status. This process was repeated every two years in the projections until 2050, and then summary variables were calculated.

Since we anticipated that the new cohorts in the future are going to have different characteristics than the current ones, we calculated and applied trends for diabetes prevalence, BMI and smoking status using data on younger cohorts from an alternative source of information, the Mexican National Health and Nutrition Surveys (ENSA 2000 and ENSANUT 2006 and 2012), a series of repeated national cross-sections in Mexico. Based on the observed/predicted characteristics (education, BMI, smoking) of the younger cohorts who will enter ages 50/51 in the future, we anticipate that future 50/51 year olds will have higher prevalence of diabetes, overweight and obesity, and also higher education than the current 2012 cohort. These trends are not shown but are available from the Technical Appendix

We implemented the FEM-Mexico simulation by loading the 50+ MHAS population in 2012, then applying the two-year transition models for mortality and incidence of health conditions (diabetes, other comorbidities, ADL's, IADL's, BMI and smoking status) with Monte Carlo decisions to calculate the new states of the population every two years. We estimated the total population by adjusting for immigration and mortality forecasts using data from the Mexican National Population Council (CONAPO) projections, and added the new 50/51 year olds to the simulation every two years. Finally, summary variables were computed.

We simulated four scenarios for the projected diabetes prevalence rates among the population 50 and older through 2050. We adopted these scenarios to estimate the potential benefits of prevention programs (20) according to the results from (23) about the efficacy of

alternative interventions, for example by changing lifestyle and using prescription drugs: 1) *Status quo*, or no-intervention. This scenario assumes that the current trends will continue, that is, current rates of e.g., smoking, obesity, other diseases, will continue unchanged. 2) 60% reduction in the incidence of diabetes starting at age 50 in 2014, assumed for every cohort entering age 50 in the future. According to the DPP, an intensive lifestyle intervention and medication (e.g., metformin) among high-risk cases could reduce the incidence of diabetes by 60%; thus we simulated a scenario under such assumption. 3) 30% reduction in two-year diabetes incidence, assuming that older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014. 4) a modest 10% reduction in two-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and economic policies are implemented to reduce diabetes risk factors starting at age 50, that, among the entering cohorts, but that the interventions impact the behaviors of all age groups starting in 2014.

The resulting number of diabetes cases for each scenario are used to estimate the consequences of future diabetes in terms of health care resources. We obtain a gross estimate of the total number of medical visits for patients with and without diabetes and, applying the cost of a medical visit, we calculated the corresponding total health care cost. In the results section, first we present the descriptive characteristics of the 50 years and older population in 2012, the starting period of the simulations. Next, we present the incidence of the health conditions between 2001 and 2003, as well as the marginal effects of the covariates for each of the equations but with a special focus on the diabetes equation and diabetes as a covariate in other equations. Finally, we present a summary of projected values for a selection of years between 2012 and 2050.

Results

Table 1 presents descriptive statistics using information just from MHAS. In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico; of these, 19.3% had been diagnosed with diabetes, 37.9% with hypertension, and the prevalence for each of the other diseases (heart attack, stroke, lung disease and cancer) was less than 5%. The percentage of the population reporting difficulty in performing at least one ADL and IADL was 12.8% and 8.9%,

respectively, and the percentage of the population reporting difficulty in performing at least one of either ADL or IADL was 16.6%. Of the total population aged 50 and older, 35.1% had normal weight, 42.8% were overweight and 22.0% were obese. The average age was 62.6 years, 46.9% were men and 53.1% women; almost half of the 50 years and older population reported less than basic schooling (0-5 years), and 1 in 10 had at least some college degree; 70% were married and 15.4% were widowed, with important differences by sex.

The 2001-2003 diabetes incidence was 4.3% and the factors significantly associated with the onset of diabetes were: education, hypertension and BMI. Higher education was associated with lower probability of having a new case of diabetes. However, this likelihood increased by 1.5% for those with hypertension, 0.8% for those living in urban environments, 1.4% for the overweight and 2.7% for the obese population. As a predictor in the equations for other diseases and health outcomes, diabetes had significant effects, increasing the two-year probability of death by 2.1%, and the two-year incidence of the following: hypertension by 3.4%, a heart attack by 0.7% and a stroke by 1.0% (See Table 2).

Regarding the results of the four simulated scenarios, Table 3 provides baseline estimates from MHAS information (2012) and the projections for the years 2020, 2030, 2040 and 2050 of the prevalence of diabetes (see also Figure 1), the total population, the total number of medical visits per year, the number of diabetics and the number of cases averted in comparison to the no-intervention scenario. The no-intervention scenario shows that the population 50 years and older is projected to increase from 20.7 million in 2012 to 48.0 million in 2050, and the prevalence of diabetes from 19.3% to 34.0%. Under the scenario of 30% reduction in two-year diabetes incidence, the total population is projected to increase to 48.6 million in 2050 and the prevalence of diabetes will be 28.6%. The projected reduction in the prevalence of diabetes is 5.4 points and in mortality 552,000 more survivors. An intermediate and perhaps more plausible scenario is the 10% reduction in two-year diabetes incidence. In this scenario, the population in 2050 will be 48.2 million and the prevalence of diabetes will be 32.3%, a 1.7 point reduction of the prevalence when compared with the no-intervention scenario. The 60% diabetes incidence reduction could lead to a 22.8% prevalence of diabetes in 2050 and 49.2 million individuals aged 50 and older.

The average age of death for the population was 75.3 years in 2012. According to the projections of the FEM-Mexico under the no-intervention scenario, the average age at death was 76.7 years in 2050; 76.8 for the scenario of 10% diabetes incidence reduction; 77.0 years for the 30% diabetes incidence reduction scenario; and 77.3 years for the 60% reduction scenario.

We turn now to the economic consequences of diabetes. Since the MHAS has no data available for the average annual cost by disease, we used a rough approximation from two other sources to gauge the difference in cost related to the presence or absence of diabetes. For Mexico and according to Rodriguez-Bolaños (5), in the Mexican Institute of Social Security (IMSS), the annual cost for a patient with diabetes was \$3,193 dollars. On the other hand, the New York State Diabetes Prevention and Control Program estimates that the average cost of a patient with diabetes is 3.5 times greater than for someone without the disease (22). We applied this ratio and obtained an average cost for a patient without diabetes in Mexico of \$912 per year.

Based on this average health care costs of the diabetic and non-diabetic population, using the projected population from the hypothetical scenarios in each group and assuming that the health care cost ratio between the diabetic and non-diabetic population will remain constant over time, we estimated the individual average yearly health care cost for the years 2012 and 2050. For example, in 2012, the total health care cost for the diabetic population was \$12,802 million (4.0 million * \$3,193) and was \$15,247 million (16.7 million * \$912) for the non-diabetic population. Adding these two amounts, we calculated \$28,049 million in total health care cost for the total population. The individual average yearly cost for 2012 was \$1,353, obtained by dividing the total health care cost by the total population (\$28,049/20.7 million). If we estimate the average health care cost at the individual level for the year 2050, in the no-intervention scenario it would be \$1,663 dollars; in the 10% diabetes incidence reduction scenario, it would be \$1,624 dollars; for the 30% reduction, it would be around \$1,544 dollars; and for the 60% reduction, the average health care cost per individual would be \$1,416 dollars (See Table 4). If we multiply the individual average health care cost by the total population, the annual savings can be obtained by comparing the result to the no-intervention scenario, representing \$1,593 million for the 10% diabetes reduction scenario, \$4,849 million for the 30% reduction scenario, and \$10,190 million for the 60% diabetes incidence reduction scenario.

We express these estimates in fiscal terms by estimating the share of the total national health expenditures that the diabetic population represents. According to the World Health Organization Global Health Expenditure database, the total expenditures in health care in Mexico was about \$28,049 million in 2012. Using figures from Table 4, in 2012 the health care cost of the diabetic population represents 45.6% (\$12,802 million /\$28,049 million) of the total health care cost. Similarly, in 2050, due to the increase in the diabetes prevalence and based on the no-intervention scenario, the health care cost of the diabetic population will represent 63.2% of the total. The equivalent share for the 10% reduction scenario would be 61.4%, compared to 57.3% share under the 30% reduction scenario, and for the 60% diabetes incidence reduction scenario, the health care cost of the diabetic population represents 49.8% of the national health care cost.

To supplement the information about the economic consequences of diabetes, we used MHAS data to estimate that, in 2012, the 50 years and older population on average had 4.9 medical visits a year; the average is much higher for individuals with diabetes (8.3) compared to the older adults without diabetes (annual average of 4.1). Our microsimulation estimates are that, in 2050, under the no-intervention scenario, the average number of medical visits would be 6.4 for the older population, 8.8 for individuals with diabetes and 5.2 for those older adults without diabetes, and the increase is mostly related to the presence of diabetes and other health conditions, for example, hypertension.

If we compare the total number of medical visits year by year for the no-intervention scenario *versus* the 10% reduction in two-year diabetes incidence, we cannot find a large difference. However, if we examine the cumulative number of avoided medical visits from 2012 to 2050, the perspective is quite different. In 2012, a medical visit in the Mexican Institute of Social Security (IMSS) costs 559 pesos (35 US dollars) (24). With the projection results, and assuming that this cost per visit remains the same in constant terms, we can roughly compare the no-intervention with the 30% incidence reduction scenario. We estimate 49.2 million avoided medical visits from 2012 through 2050, which represents \$2,047 million in savings. Similarly, we estimate 547,543 avoided medical visits between 2014 and 2016, representing \$10.4 million dollars in savings (data not shown).

Similarly, we estimate the number of cases that could be averted if we could reduce the incidence/prevalence of diabetes. When comparing the no-intervention scenario to the 30% diabetes incidence reduction scenario (with, say, lifestyle modification), we calculate for the year 2020, a total of 816,320 annual averted cases of diabetes, and for the year 2050, 2.5 million. If we compare no-intervention with the 60% diabetes incidence reduction scenario (with metformin plus lifestyle modifications), the averted cases of diabetes would be 1.6 million in 2020 and 5.4 million in 2050 (see Figure 2).

Discussion

In the present study we projected the diabetes prevalence in Mexico under four scenarios of diabetes incidence reduction: no-intervention, and hypothetical interventions that would reduce incidence 0%, 30% and 60%. Our simulation results, from 2012 through 2050, underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions, which drive a significant rise in health care costs. We provide estimates of the impact that a reduction in the diabetes incidence could represent for the public health system in terms of the amount of population without diabetes and the corresponding savings in health care costs.

The analysis of specific diabetes prevention interventions is beyond the scope of our paper, but previous authors have contributed vastly to this body of evidence. The Diabetes Prevention Program and other research studies using medical trials had found that interventions to reduce the incidence of diabetes could delay the onset of the disease and reduce its prevalence by 10-60% depending on the duration of the interventions and the strategies used, ranging from lifestyle changes to prescribed drugs, or a combination of both. We choose to apply the results from the DPP to the FEM-Mexico scenarios because the program focuses on lifestyle modification and Mexico is promoting public policies to change diet and increase exercise among the population; also, the DPP recommended the use of metformin, a drug proven to delay the onset of diabetes, whose low cost makes it applicable in Mexico. This body of research suggests that public policies could focus on lifestyle modification, weight loss and increased

physical activity to prevent or delay diabetes (25). These clinical trials have identified the variety of interventions and the heterogeneity of their effectiveness; the upper limit of the scenarios we used in our simulations may be difficult to achieve in clinical practice or at the population level because of the heterogeneity in the characteristics and preferences of individuals (26). Nevertheless, the evidence shows that the interventions intended to delay diabetes result in significant savings and should be prioritized. In addition, these studies highlight the importance of interventions that identify individuals at the highest risk of developing diabetes, in order to maximize the effectiveness of interventions and minimize side-effects of interventions with prescribed drugs. While personalized or tailored treatment may not be feasible for the general population as a whole, it could represent great gains if applied to certain population groups: for example, those identified at the highest risk of developing diabetes. Thus, tools to identify those at the highest risk may be highly relevant in countries with limited resources like Mexico.

Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes. These potential savings represent a rough estimate and may be a lower bound, since we have not considered the benefits of reducing diabetes to the families, economic productivity and the gains in quality of lives of the individuals involved. Certainly, projections such as the ones we present can serve to raise awareness about major trends with population aging that may affect health, and thus social and economic development (27). The projected scenarios illustrate the future burden of the disease if current trends continue unchanged, as well as the potential beneficial effects if interventions to reduce diabetes prevalence are implemented.

The limitations of the study are related to the nature of the data from the Mexican Health and Aging Study. For example, the analysis is based on self-reported data and may not fully represent the prevalence of diabetes (28), and the model's use of only two waves of information to estimate disease transitions may potentially impact the reliability of results.

The acceleration of population aging in the coming decades will play a key role in the burden of the disease (4), as older adults are more likely to develop diabetes than younger adults, and mortality among people with diabetes is declining. These two factors, combined with better technology to manage the disease, may increase the prevalence of diabetes and the years spent

with the disease. Obesity trends are also important. The current epidemic of obesity in Mexico implies that the health care system needs to quantify the future high cost of the *status quo*. Our estimates show that, if left unchanged, the prevalence of diabetes will reach unprecedented growth by 2050. Thus, diabetes is projected to be one of the major challenges for the Mexican aging society, given its prevalence, the associated risk factors, the genetic predisposition of the Mexican population, the high cost of health care and family care for the disease, and other economic and health consequences. We hope to have contributed to the knowledge of the potential trends and benefits of diabetes prevention and control interventions that can begin now, and that this information can prove to be of assistance to decision makers.

Contributors: Cesar Gonzalez Gonzalez (CGG), Bryan Tysinger (BT), Rebeca Wong (RW) and Dana P Goldman (DG) made substantial contributions to the conception and design of the paper. BT assisted with analysis and interpretation of data for this manuscript. CGG analyzed the data, and drafted and revised the paper. RW, BT and DG revised the draft paper critically for important intellectual content. All authors approved of the final version to be published. CGG is the guarantor.

Funding: This study was funded by grants from the National Institute on Aging. The funders had no input into the selection or analysis of data or the content of the final manuscript.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: support from the National Institute of Aging (Grants P30AG024968 and R01AG025533); Dr. Goldman is a founder of Precision Health Economics, a consultancy that provides services to the life sciences industry; and no other relationships or activities that could appear to have influenced the submitted work.

Transparency: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing statement: The MHAS is a public use data set that can be obtained from the MHAS webpage http://www.mhasweb.org/

"I Cesar Gonzalez-Gonzalez The Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs within and any related or stand alone film submitted (the Contribution") has the right to grant on behalf of all authors and does grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licencees, to permit this Contribution (if accepted) to be published in the BMJ and any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence set out at: http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-open-access-and-permission-reuse."

Please tick **one or more** boxes as appropriate:

I am the sole author of the Contribution.
I am one author signing on behalf of all co-owners of the Contribution.
The Contribution has been made in the course of my employment and I am signing as
authorised by my employer. I am a US Federal Government employee acting in the course of my employment. I am not a US Federal Government employee, but some or all of my co-authors are. I am an employee of the UK Crown* acting in the course of my employment I am a US Federal Government employee acting in the course of my employment. I am not a US Federal Government employee, but some or all of my co-authors are. I am an employee of the UK Crown acting in the course of my employment I am not an employee of the UK Crown acting in the course of my employment but some/all of my co-authors are.*

Bibliography

- 1. OECD. Cardiovascular Disease and Diabetes: Policies for Better Health and Quality of Care. 2015.
- 2. Arredondo A, De Icaza E. Costos de la Diabetes en América Latina: Evidencias del Caso Mexicano. Value Heal. 2011;14(5 SUPPL.):S85–8.
- 3. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, et al. Ensanut 2012Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. [Internet]. Instituto Nacional de Salud Pública. Cuernavaca; 2012. Available from: http://ensanut.insp.mx/informes/ENSANUT2012ResultadosNacionales.pdf
- 4. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr [Internet]. 2010;8(1):29. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20969750%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC2984379
- 5. Rodríguez Bolaños R, Reynales Shigematsu LM, Jimenez Ruiz JA, Juárez Márquez SA, Hernández Ávila M. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2010;28(6):412–20.
- 6. OECD. Projecting OECD Health and Long-Term Care Expenditures: What Are the Main Drivers? 2006.
- 7. Rull J, Aguilar-Salinas C, Rojas R, Rios-Torres JM, Gómez-Pérez FJ, Olaiz G. Epidemiology of type 2 diabetes in Mexico. Vol. 36, Archives of Medical Research. 2005. p. 188–96.
- 8. IDF. Diabetes Atlas. Seventh Edition. 2015.
- 9. Mata M, Antoñanzas F, Tafalla M, Sanz P. El coste de la diabetes tipo 2 en España. Gac Sanit. 2002;16(6):511–20.
- 10. Agudelo-Botero M, Dávila-Cervantes CA. Carga de la mortalidad por diabetes mellitus en América Latina 2000-2011: los casos de Argentina, Chile, Colombia y México. Gac Sanit [Internet]. 2015;29(3):172–7. Available from: http://dx.doi.org/10.1016/j.gaceta.2015.01.015
- 11. Aguilar-Salinas CA. Diabetes y tuberculosis: En el laberinto del subdesarrollo. Rev

- Investig Clin. 2005;57(1):82–4.
- 12. Bertram MY, Lim SS, Barendregt JJ, Vos T. Assessing the cost-effectiveness of drug and lifestyle intervention following opportunistic screening for pre-diabetes in primary care. Diabetologia. 2010;53(5):875–81.
- 13. Pinto G, Beltrán-sánchez H. Prospective study of the link between overweight / obesity and diabetes incidence among Mexican older adults: 2001-2012. Salud Publica Mex. 2015;57(1):s15–21.
- 14. Rtveladze K, Marsh T, Barquera S, Sanchez Romero LM, Levy D, Melendez G, et al. Obesity prevalence in Mexico: impact on health and economic burden. Public Health Nutr. 2014;17(1):233–9.
- 15. Wolf DA. Synthetic Trajectories obtained by matching longitudinal data. 2014.
- 16. Zucchelli E, Jones A, Rice N. The evaluation of health policies through dynamic microsimulation methods. UK; 2012.
- 17. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: A systematic review. Diabetes Care. 2010;33(8):1872–94.
- 18. Knowler W, Barret-Connor E, Fowler S, Hamman R, Lachin J, Walker E, et al. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. N Engl J Med [Internet]. 2002 Feb 7;346(6):393–403. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa012512
- 19. Goldman DP, Zheng Y, Girosi F, Michaud PC, Olshansky SJ, Cutler D, et al. The benefits of risk factor prevention in Americans aged 51 years and older. Am J Public Health. 2009;99(11):2096–101.
- 20. Olshansky SJ, Goldman DP, Zheng Y, Rowe JW. Aging in America in the Twenty-First Century: Demographic Forecasts from the MacArthur Foundation Research Network on an Aging Society Published by: Wiley on behalf of Milbank Memorial Fund content in a trusted digital archive. We use information techn. Milbank Q. 2013;87(4):842–62.
- 21. Goldman DP, Lakdawalla D, Michaud P, Eibner C, Zheng Y, Gailey A, et al. The Future Elderly Model: Technical Documentation. 2015.
- Wong R, Michaels-Obregon A, Palloni A. Cohort Profile: The Mexican Health and Aging Study (MHAS). Int J Epidemiol. 2015;1–10.
- 23. Gregg EW, Boyle JP, Thompson TJ, Barker LE, Albright AL, Williamson DF. Modeling the impact of prevention policies on future diabetes prevalence in the United States: 2010-2030. Popul Health Metr. 2013;11(1):18.
- 24. Rodríguez Bolaños RDLÁ, Reynales Shigematsu LM, Jiménez Ruíz JA, Juárez Márquezy SA, Hernández Ávila M, Jimenez Ruiz JA, et al. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2010;28(6):412–20.
- 25. Guthrie DW. The Prevention or Delay of Type 2 Diabetes. Clin Diabetes. 2002 Jul 1;20(3):109–16.

- 26. Dorresteijn JAN, Visseren FLJ, Ridker PM, Wassink AMJ, Paynter NP, Steyerberg EW, et al. Estimating treatment effects for individual patients based on the results of randomised clinical trials. BMJ. 2011;343:d5888.
- 27. Imhoff E van, Post W. Microsimulation Methods for Population Projection. Popul An English Sel. 2008;10(1):97–138.
- 28. Kumar A, Wong R, Ottenbacher KJ, Al Snih S. Prediabetes, undiagnosed diabetes, and diabetes among Mexican adults: Findings from the Mexican Health and Aging Study. Ann Epidemiol. 2016;26(3):163–70.



Table 1. Characteristics of the population 50 years and older, MHAS 2012

	%
Age (mean)	62.6
Sex (male)	46.9
Education	
Less than complete basic (0 to 5 years)	46.4
Basic complete (6 years)	20.8
High school (7 to 12 years)	22.8
College (13+ years)	10.0
Marital Status	
Single	5.1
Married	69.8
Separated/Divorced	9.6
Widowed	15.5
Chronic diseases (% Yes)	
Hypertension	37.9 19.4 1.2 3.0 5.1 2.2
Diabetes	19.4
Cancer	1.2
Heart attack	3.0
Lung disease	5.1
Stroke	2.2
Disability (%)	
Any ADL (1+)	12.9
Any IADL (1+)	11.7
Any ADL or Any IADL	19.3
Body Mass Index (BMI)	
Normal (< 25.00 kg/m ²)	35.1
Overweight (25.00 to 29.99 kg/m²)	42.9
Obese 1 (30.00 to 34.99 kg/m²)	16.7
Obese 2 (35.00 to 39.99 kg/m²)	3.8
Obese 3 (≥40 kg/m²)	1.6
Smoking Status	
Never	63.7

Former	23.4
Current	13.0

Source: MHAS 2012. Weighted statistics.



Table 2: Incidence equations for mortality, chronic diseases, smoking status and BMI for the population 50 years and older, FEM-Mexico 2001-2003 (Marginal effects)

				Heart		Lung		Smoke	Log
	Mortality	Diabetes	Hypertension	attack	Cancer	Disease	Stroke	(Current)	BMI
TWO YEAR INCIDENCE	2.3	4.3	16.1	1.4	0.4	2.7	0.5	8.5	3.3
	Marginal effects								
Lag age 50-64	0.002	-0.001	0.003	0.001	0.000	0.001	0.000	-0.003	0.002
Lag age 65-74	0.001	-0.002	-0.002	0.001	0.000	0.000	0.001	-0.001	-0.004
Lag age 75+	0.003	0.000	-0.001	0.000	-0.001	0.001	0.000	-0.004	0.000
Male	0.017	0.004	-0.049	0.004	0.000	-0.001	-0.001	0.124	-0.004
Basic school	0.005	0.021	-0.039	-0.009	0.005	-0.014		-0.023	0.028
Highschool	0.012	-0.030	-0.005	-0.002	0.006	-0.007	0.005	0.015	0.005
College	-0.013	-0.019	-0.042	0.005	0.006	-0.012	-0.003	0.011	0.012
Lag Hypertension	0.003	0.015		0.016			0.004	-0.036	0.007
Lag Diabetes	0.021		0.034	0.007			0.010	-0.019	-0.003
Lag Heart attack	0.017						0.002	-0.021	0.013
Lag Cancer	0.074						-0.002	-0.010	-0.001
Lag Lung Disease	0.011							0.005	-0.003
Lag Stroke	0.027							-0.025	0.001
Lag 1 IADL	0.001							-0.019	-0.001
Lag 2+ IADL	0.000							-0.036	-0.014
Lag 1 ADL	0.013							0.014	0.001
Lag 2 ADL	0.057							0.035	0.008
Lag 3+ ADL	0.154							0.038	0.014
Lag Former smoker	0.003	-0.010		0.003	0.002	-0.002	0.003		0.002
Lag Widowed	0.012	-0.005		-0.001	-0.002	0.002	-0.001	0.014	0.000
Lag NOT Exercise	0.013	0.008	0.020	0.007	0.001	0.006	0.002	0.120	0.010
More urban locality	0.005	0.007	-0.008	-0.003	0.001	-0.010	0.001	0.014	0.017
Lag BMI less than 30	0.042	0.111	0.114	0.008					0.968
Lag BMI 30 or higher	0.030	0.040	0.186	-0.008					0.616

Table 3: Projection of prevalence of diabetes, total population and number of medical visits by Simulation Scenarios, Population 50 years and older, FEM-Mexico simulation 2012-2050

ESTIMATE by SCENARIO	2000	2006	2012	2020	2030	2040	2050
Diabetes prevalence (%)							
Observed	12.00	15.74	19.34				
No intervention			19.34	26.24	30.69	32.91	34.00
10% incidence reduction			19.34	25.23	29.29	31.29	32.25
30% incidence reduction			19.34	23.32	26.27	27.74	28.64
60% incidence reduction			19.34	20.42	21.35	22.05	22.76
Total Population							
No intervention			20,727,415	26,781,877	34,641,639	41,652,429	48,010,723
10% incidence reduction			20,727,415	26,794,525	34,705,941	41,774,461	48,180,921
30% incidence reduction			20,727,415	26,814,809	34,832,223	42,027,492	48,563,485
60% incidence reduction			20,727,415	26,851,575	35,021,745	42,468,762	49,191,108
Number of medical visits (A	nnual)						
No intervention			102,183,113	151,881,059	216,505,084	274,138,503	324,866,875
10% incidence reduction			102,183,113	151,328,257	215,568,988	273,165,155	323,819,400
30% incidence reduction			102,183,113	150,258,034	213,441,667	270,708,771	321,751,070
60% incidence reduction			102,183,113	148,650,611	209,909,778	267,031,679	318,180,682
Number of diabetics (Annua	I)						
No intervention			4,009,290	7,364,738	11,155,124	14,407,673	17,209,864
10% incidence reduction			4,009,290	7,083,003	10,660,831	13,737,582	16,380,310
30% incidence reduction			4,009,290	6,548,418	9,587,597	12,240,966	14,648,013
60% incidence reduction			4,009,290	5,736,938	7,826,970	9,816,176	11,773,857
Averted cases of diabetes							
(vs. no-intervention)				201 = 2 =	40.4.055	0=0.055	
10% incidence reduction			-	281,735	494,293	670,092	829,554
30% incidence reduction			-	816,320	1,567,527	2,166,708	2,561,851
60% incidence reduction			-	1,627,799	3,328,153	4,591,497	5,436,007

Table 4: Projection of total population, percentage, and health care cost by diabetes status, population aged 50 and older, FEM-Mexico simulation 2012-2050

Chavastavistica	2012	2050						
Characteristics	2012	No intervention	10% reduction	30% reduction	60% reduction			
Total Population	20,727,415	48,010,723	48,180,921	48,563,485	49,191,108			
Proportion of population by Diabetes diagnosis								
With	19.34	34.00	32.25	28.64	22.76			
Without	80.66	66.00	67.75	71.36	77.24			
Total Population by Diabetes Condition								
With	4,009,290	15,797,928	15,031,288	13,451,263	10,858,373			
Without	16,718,125	32,212,795	33,149,633	35,112,222	38,332,735			
Total Health care costs by diabetes condition								
With	12,801,662,970	50,442,784,104	47,994,902,584	42,949,882,759	34,670,784,989			
Without	15,246,930,000	29,378,069,040	30,232,465,296	32,022,346,464	34,959,454,320			
Total	28,048,592,970	79,820,853,144	78,227,367,880	74,972,229,223	69,630,239,309			
Individual average Health care cost	1,353	1,663	1,624	1,544	1,416			

Figure 1: Diabetes Prevalence for Scenarios of Diabetes Incidence Reduction, Population aged 50 and older, FEM-Mexico 2012-2050

Figure 2. Number of averted DIABETES cases, No intervention scenario vs 30% and 60% diabetes incidence reduction, FEM-Mexico



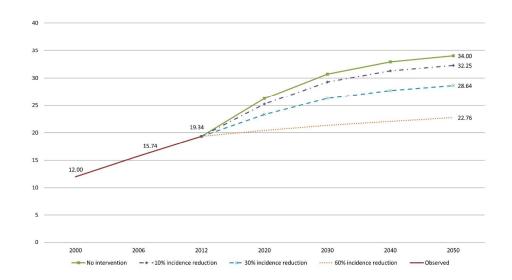


Figure 1: Diabetes Prevalence for Scenarios of Diabetes Incidence Reduction, Population aged 50 and older, FEM-Mexico 2012-2050

338x190mm (300 x 300 DPI)

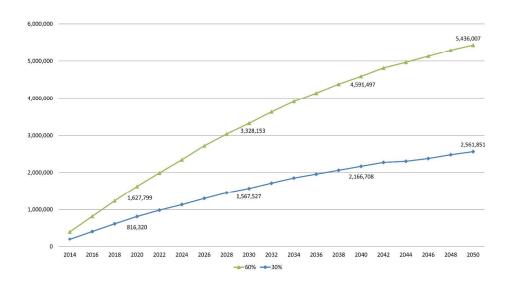


Figure 2. Number of averted DIABETES cases, No intervention scenario vs 30% and 60% diabetes incidence reduction, FEM-Mexico

338x190mm (300 x 300 DPI)

Modeling Diabetes and Related Medical Care of the Future Elderly in Mexico

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

Technical Appendix

Structure of the microsimulation model

The structure of the FEM-Mexico microsimulation and the differences with the HRS-FEM are presented in the Appendix Figure 1. Our simulation starts in 2012 with 20.7 Million individuals age 50+ (17.7% of the population in 2012; (CONAPO, 2012)). The simulation model estimates the risk of developing diabetes, other five chronic diseases and the survival status for each individual. Due to the structure of the model, every two years the microsimulation model updates the health status and mortality risk for each individual. To replenish the youngest cohorts, a new cohort of 50 and 51 year-old individuals are added at the beginning of each simulated cycle.

This technical appendix describes only the adaptations made to the FEM in order to work with the Mexican Health and Aging Study (MHAS), in depth details of the FEM are published everywhere (add reference).

The model's main variables are age, gender, smoke, BMI and six chronic conditions (hypertension, diabetes, heart disease, lung disease, stroke and cancer). We also create an indicator variable mortality. The baseline cohort is defined at the initial period (2001). This time period represents the first two years of the simulations (i.e., 2012 and 2013). The variables age, gender, smoke, BMI and chronic conditions are sampled from MHAS with replacement. These samples are repeated until the number of individuals in each age and sex category are equal to the Mexican population distribution in 2012.

After establishing the baseline cohort, the microsimulation iterates to the next time period by projecting the values of each variable for the next two years (i.e., 2014 and 2015). Since the 50 and 51 years individuals age to 52 and 53 years-old, respectively, at time 2, new 50 and 51 year-old individuals are added to the simulation to replenish the youngest age group. The characteristics of these new individuals are sampled with replacement from the 50-51 year-old individuals in MHAS 2012, weighted by the age- and gender-specific projected population of 50 year-olds based on the official Mexican projections (CONAPO) and imposing the trends for some of the main variables.

MHAS provides self-reported chronic conditions for each individual in 2001, 2003 and 2012. We use logistic regressions to estimate the probability of transitioning to one of the six mutually exclusive health states in 2003 based on not having that chronic condition in 2001, controlling for demographic and comorbid conditions in 2001. Then we projected transitions of self-reported diabetes, hypertension, heart attack, cancer, stroke and lung disease. The independent variables

include health status measures and basic demographic characteristics such as age, gender, smoking status or weight category, as measured at baseline in 2001. The coefficient estimates of these transitions models predict health status two years into the future (2003). All chronic conditions are treated as absorbing states.

Specific situations for FEM-Mexico

a. Inter-wave gap period

The first difference between the structure of the FEM-Mexico and the FEM was that in the latter, the main source of information, the Health and Retirement Study (HRS), is collected every two years and the microsimulation uses this gap time to estimate health status of the individuals. In MHAS there is three available waves, 2001, 2003 and 2012 with different inter-wave periods. We had to choose our baseline population based on the advantages that the microsimulation model presents and we decided to use the 2012 data as a baseline and the 2001-2003 information to estimate the health transitions and to run our microsimulation.

b. Cross-validation: Cohort analysis (MHAS 2003-2011/2013)

The next step was to corroborate that adapting the MHAS information to the FEM could lead to acceptable forecast of diabetes, to do so we run a cohort analysis using wave 2 (2003) as the start point of the simulation, then we compare the results obtained from the FEM-Mexico with the real data from MHAS wave 3 (2012). Results show that FEM-Mexico predicts effectively the prevalence of diabetes (see figure 2).

- c. Demographic adjustments to run the simulation
- 1) Since age and sex distribution in the MHAS differs from the CONAPO projections we reweight the population by age and sex to have a common start point for the projections (see Figure 3).
- 2) Using the CONAPO projections (2010-2050) we made some adjustments on mortality probabilities and due to evident differences by age group we adjust for two groups: 50 to 64 years and 65 years and older, all calculations relative to 2012 level (see table 1)
- 3) Migration adjustments [by year (2013-2050) single age and sex], all calculations relative to 2012 level.
 - d. Incoming cohorts (new 50-51 years old)

We assume that the new 50-51 years old individuals will be different in several characteristics. For example, with respect to the actual cohorts, they will be more educated, with lower tobacco and alcohol consumption and with higher BMI. Using information from the Mexican National Health

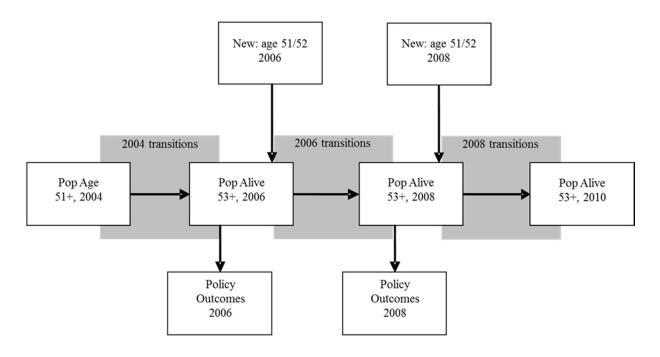
Surveys (2000, 2006 and 2012) we predicted trends for these variables and applied them to the incoming cohorts (50-51 years old).

e. Missing data.

We used records in which the information for all the variables is complete.



Figure 1. **Architecture of the FEM**



HRS-FEM and FEM-Mexico differences

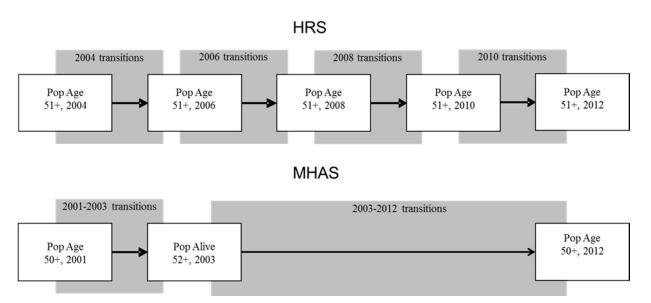
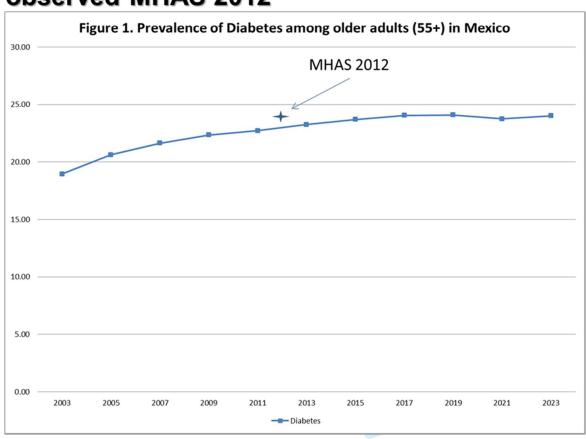


Figure 2.

Comparison between microsimulation and observed MHAS 2012



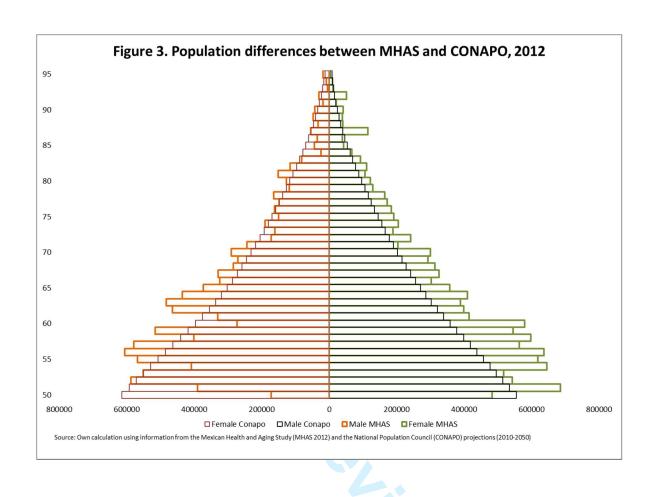


Table 1. Trends for mortality, diabetes, Body Mass Index and Smoking, 2012-2050

Year	Mortality a	adjustments ¹	Diabetes ²	Body Mass Index ²				Smoking ²		
Teal	50-64	65+	Diabetes	Overweight	Obese 1	Obese 2	Obese 3	Current	Former	
2012	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	
2013	0.9920	0.9983	1.0176	1.0007	1.0119	1.0196	1.0458	1.0309	0.9856	
2014	0.9838	0.9962	1.0354	1.0014	1.0239	1.0396	1.0935	1.0624	0.9714	
2015	0.9756	0.9934	1.0534	1.0020	1.0359	1.0599	1.1433	1.0947	0.9573	
2016	0.9671	0.9901	1.0718	1.0027	1.0480	1.0806	1.1952	1.1277	0.9434	
2017	0.9585	0.9861	1.0904	1.0034	1.0602	1.1015	1.2492	1.1614	0.9296	
2018	0.9498	0.9817	1.1092	1.0041	1.0725	1.1229	1.3056	1.1959	0.9160	
2019	0.9407	0.9769	1.1283	1.0048	1.0848	1.1445	1.3642	1.2310	0.9026	
2020	0.9317	0.9718	1.1477	1.0055	1.0971	1.1665	1.4253	1.2669	0.8892	
2021	0.9227	0.9666	1.1674	1.0061	1.1096	1.1889	1.4888	1.3035	0.8761	
2022	0.9138	0.9614	1.1873	1.0068	1.1220	1.2116	1.5549	1.3408	0.8630	
2023	0.9051	0.9563	1.2075	1.0075	1.1346	1.2347	1.6237	1.3788	0.8502	
2024	0.8965	0.9515	1.2279	1.0082	1.1472	1.2581	1.6952	1.4175	0.8374	
2025	0.8882	0.9470	1.2487	1.0089	1.1598	1.2819	1.7695	1.4569	0.8249	
2026	0.8802	0.9428	1.2697	1.0096	1.1725	1.3061	1.8467	1.4969	0.8124	
2027	0.8722	0.9388	1.2909	1.0103	1.1852	1.3306	1.9268	1.5377	0.8002	
2028	0.8641	0.9351	1.3125	1.0109	1.1980	1.3555	2.0100	1.5791	0.7880	
2029	0.8561	0.9316	1.3343	1.0116	1.2109	1.3807	2.0964	1.6212	0.7760	
2030	0.8480	0.9282	1.3564	1.0123	1.2238	1.4064	2.1859	1.6640	0.7642	
2031	0.8400	0.9251	1.3788	1.0130	1.2367	1.4324	2.2787	1.7074	0.7525	
2032	0.8319	0.9221	1.4014	1.0137	1.2497	1.4588	2.3749	1.7514	0.7409	
2033	0.8236	0.9195	1.4244	1.0144	1.2627	1.4855	2.4744	1.7960	0.7295	
2034	0.8149	0.9172	1.4476	1.0150	1.2757	1.5126	2.5775	1.8412	0.7182	
2035	0.8058	0.9153	1.4711	1.0157	1.2888	1.5402	2.6841	1.8870	0.7071	
2036	0.7962	0.9138	1.4949	1.0164	1.3019	1.5681	2.7943	1.9334	0.6961	
2037	0.7866	0.9128	1.5189	1.0171	1.3150	1.5963	2.9082	1.9803	0.6852	
2038	0.7766	0.9124	1.5432	1.0178	1.3282	1.6250	3.0259	2.0277	0.6745	
2039	0.7660	0.9125	1.5678	1.0185	1.3414	1.6540	3.1472	2.0757	0.6639	
2040	0.7551	0.9133	1.5927	1.0192	1.3546	1.6835	3.2724	2.1241	0.6535	
2041	0.7439	0.9146	1.6179	1.0198	1.3678	1.7133	3.4015	2.1730	0.6431	
2042	0.7327	0.9163	1.6433	1.0205	1.3811	1.7434	3.5344	2.2223	0.6330	
2043	0.7216	0.9183	1.6690	1.0212	1.3944	1.7740	3.6712	2.2721	0.6229	
2044	0.7106	0.9206	1.6950	1.0219	1.4077	1.8050	3.8119	2.3222	0.6130	
2045	0.6997	0.9234	1.7213	1.0226	1.4210	1.8363	3.9565	2.3727	0.6032	
2046	0.6892	0.9267	1.7478	1.0233	1.4343	1.8680	4.1050	2.4235	0.5936	
2047	0.6791	0.9303	1.7746	1.0239	1.4477	1.9001	4.2574	2.4747	0.5841	
2048	0.6694	0.9340	1.8017	1.0246	1.4610	1.9326	4.4136	2.5261	0.5747	
2049	0.6600	0.9376	1.8290	1.0253	1.4744	1.9655	4.5737	2.5778	0.5654	
2050	0.6517	0.9419	1.8566	1.0260	1.4877	1.9987	4.7376	2.6297	0.5563	

¹ Trends calculated using CONAPO Projections (2010-2050)

 $^{^{\}rm 2}$ Trends calculated using Mexican National Health Surveys (2000, 2006 and 2012)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	Projecting diabetes among older adults in Mexico: The Future Elderly Model-Mexico (FEM-Mexico)	1
		Objective: To estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes Design: A simulation study using longitudinal data from the Mexican Health and Aging Study (MHAS) and adapting the Future Elderly Model (FEM) to simulate scenarios of hypothetical interventions that would reduce diabetes incidence. Participants: Data from 14,662 participants with information on self-reported diabetes, demographic and health characteristics, and mortality. Outcome measures: We obtained, for each scenario of diabetes incidence reduction, the following summary measures for the population aged 50 years and older from 2012-2050: prevalence of diabetes, total population with diabetes, number of medical visits Results: In 2012, there were approximately 20.7 million persons aged 50 years and older in Mexico;, 19.3% had been diagnosed with diabetes; and the 2001-2003 diabetes incidence was 4.3%. The no-intervention scenario shows that the prevalence of diabetes is projected to increase from 19.3% in 2012 to 34.0% in 2050. Under the 30% incidence reduction scenario, the prevalence of diabetes will be 28.6% in 2050. Comparing the no-intervention scenario with the 30% and 60% diabetes incidence reduction scenarios, we estimate a total of 816,320 and 1.6 million annual averted cases of diabetes, respectively, for the year 2020. Limitations: The limitations are related to the nature of the data from the Mexican Health and Aging Study, since the analysis is based on self-reported data and maybe underestimate the prevalence of diabetes. Discussion: Our study underscores the importance of diabetes as a disease by itself, but also the potential health care demands and social burden of this disease and the need for policy interventions to reduce diabetes prevalence	2
Introduction			
Background/rationale	2	Diabetes represents a major health problem and a significant burden on health care systems and societies overall. This is particularly the case in countries like Mexico, where the prevalence of diabetes among the population 20-79 years old was 15.9% in 2011. Population aging and the growing prevalence of diabetes raise concerns about the increased burden on social, health and family systems because of the known consequences of this disease –health complications, greater social needs, loss in productivity and earnings and diminished quality of life. From a public policy perspective, it is important to take a glance into the future burdens and understand how the prevalence of diabetes will change over the next decades.	4-5

		One way to assess the future burden of the disease is to use microsimulation models, these models can be used to evaluate	
		the impact of interventions under alternative scenarios.	
Objectives	3	To estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health	6
		and economic burden of diabetes	
Methods			
Study design	4	We modeled the trajectory of future diabetes in Mexico from 2012 to 2050 using a microsimulation model, the Future	6
		Elderly Model (FEM). We construct four scenarios for the projections, estimating the effect of reducing two-year diabetes	
		incidence rates by 0%, 10%, 30% and 60%. We selected the scenarios based on evidence from clinical trials, with effects	
		from as large as that in the clinical trial setting to more attenuated. The microsimulation model takes into account the	
		current prevalence, the estimated new cases of diabetes (incidence) among those aged 50 and older in each two-year	
		period, the deaths among the group 50 and older in each two-year period, and the prevalence among the new population	
		entering the group 50 and older in each two-year period in the future.	
Setting	5	The individual level data comes from the Mexican Health and Aging Study (MHAS), a prospective survey of a nationally and	7
		urban-rural representative sample of adults aged 50 years and older residing in Mexico in 2001. We used three waves of	
		available data: 2001, 2003 and 2012. A refresher sample of individuals aged 50-61 was added in 2012, to once again	
		represent the population aged 50 and older in 2012.	
Participants	6	The baseline survey, in 2001, included a nationally representative sample of Mexicans aged 50 and over and their	7
		spouse/partners regardless of their age. A direct interview was sought with each individual and proxy interviews were	
		obtained when poor health or temporary absence precluded a direct interview.	
Variables	7	To measure diabetes prevalence, MHAS respondents were asked: "Has a doctor or medical personnel ever told you that	8
		you have diabetes or a high blood sugar level?" The equation for the 2001 to 2003 diabetes incidence was used to estimate	
		the probability of developing diabetes, using a probit regression model with covariates measured in 2001: age, gender,	
		education, marital status, ever hypertension, body mass index, smoking status, physical activity in the last two years, size of	
		locality of residence and health insurance. To estimate the incidence equation, only the cases that reported no diabetes in	
		2001 are included in the analytical sample.	
Data sources/	8*	We simulated four scenarios for the projected diabetes prevalence rates among the population 50 and older through 2050.	9
measurement		We adopted these scenarios to estimate the potential benefits of prevention programs (20) according to the results from	
		(23) about the efficacy of alternative interventions, for example by changing lifestyle and using prescription drugs: 1) Status	
		quo, or no-intervention. This scenario assumes that the current trends will continue, that is, current rates of e.g., smoking,	
		obesity, other diseases, will continue unchanged. 2) 60% reduction in the incidence of diabetes starting at age 50 in 2014,	
		assumed for every cohort entering age 50 in the future. According to the Diabetes Prevention Program, an intensive	

		lifestyle intervention and medication (e.g., metformin) among high-risk cases could reduce the incidence of diabetes by 60%; thus we simulated a scenario under such assumption. 3) 30% reduction in two-year diabetes incidence, assuming that	
		60%; thus we simulated a scenario under such assumption. 3) 30% reduction in two-year diabetes incidence, assuming that	
		older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014. 4) a modest 10%	
		reduction in two-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and	
		economic policies are implemented to reduce diabetes risk factors starting at age 50, that is, among the entering cohorts,	
		but that the interventions impact the behaviors of all age groups starting in 2014.	
Bias	9	We estimated the total population by adjusting for immigration and mortality forecasts using data from the Mexican	9
		National Population Council (CONAPO) projections. For the new cohorts we calculated and applied trends for diabetes	
		prevalence, BMI and smoking status using data on younger cohorts from an alternative source of information, the Mexican	
		National Health and Nutrition Surveys (ENSA 2000 and ENSANUT 2006 and 2012), a series of repeated national cross-	
		sections in Mexico.	
Study size	10	14, 662 individuals with complete information on all the included variables in the analysis. A fixed available sample.	
Quantitative variables	11	The variables in the analysis were coded as follow: age (50-64, 65-74, 75+ years), education (less than basic, basic, high	
		school and college), marital status (single, married, separated/divorced, widowed), body mass index (BMI	
		underweight/normal [lower than 25.0], overweight [25.0-29.9], obese [30 or higher]), smoking status (never, current, or	
		former), size of locality of residence (less than 100,000 inhabitants, 100,000 or more inhabitants), limitations with five	
		Activities of Daily Living (ADL's) (none, one, two, three or more) and four Instrumental Activities of Daily Living (IADL's)	
		(none, one, two or more).	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-9
		We used microsimulation models to 1) produce individual trajectories, that is, 2 year transitions, and estimate incidence for	
		a number of health conditions and disability statuses; and 2) ensure that the data remains representative of the population	
		aged 50 years and older into the future by replenishing the sample, with 50-51 year olds incorporated into the sample every	
		two years.	
		We used probit regression models to estimate the probability of developing diabetes. Since the FEM works as a	
		simultaneous equation model we also estimated similar incidence equations using probit regression models for self-	
		reported hypertension, cancer, heart attack, lung disease, stroke and mortality; ordered probit models for smoking status,	
		limitations with five Activities of Daily Living (ADL's) and four Instrumental Activities of Daily Living (IADL's) and linear	
		regression models for log (BMI).	
		We estimated an OLS equation for the number of medical visits as a dependent variable, including with/without diabetes as	
		the main explanatory variable.	
		(b) Describe any methods used to examine subgroups and interactions	

		(c) Explain how missing data were addressed –	
		For BMI - one of the key explanatory variables - we imputed the missing values using STATA.	
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed The baseline survey is a national representative survey of individuals born prior to 1951. The baseline survey was conducted in 2001, and a follow-up visit to the same individuals was conducted in 2003. The sample for the MHAS baseline was selected from residents of both rural and urban areas, from the National Employment survey (Encuesta Nacional de Empleo, ENE), carried out by the INEGI (Instituto Nacional de Estadistica y Geografia) in Mexico; 11,000 households with at least one resident of age 50 or older were eligible to be part of the MHAS baseline sample. A follow-up visit was completed in 2012. The sample was refreshed by adding a representative sample of the population from the 1952-1962 birth cohorts, as well as their spouses/partners regardless of age. Similar to the baseline interview, the	
		sampling frame for the new cohort sample was the Mexican National Employment and Occupation Survey (ENOE, previously named National Employment Survey, ENE) 2012. During the 2012 survey, 18,465 interviews were completed, including 2,742 next-of-kin interviews. (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	See Table 1.	21
Outcome data	15*	See Table 3.	23
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included See Tables 2, 3 and 4, and Figures 1 and 2	22-26
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses See Technical appendix	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14

		We projected the diabetes prevalence in Mexico under four scenarios of diabetes incidence reduction: no-intervention, and hypothetical interventions that would reduce incidence by 10%, 30% and 60%. Our simulation results, from 2012 through 2050, underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions. Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes.	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias The limitations of the study are related to the nature of the data from the Mexican Health and Aging Study. For example, the analysis is based on self-reported data and may not fully represent the prevalence of diabetes, and the model's use of only two waves of information to estimate disease transitions may potentially impact the reliability of results.	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Our estimates show that, if left the prevalence of diabetes will reach unprecedented growth by 2050. Thus, diabetes is projected to be one of the major challenges for the Mexican aging society, given its prevalence, the associated risk factors, the genetic predisposition of the Mexican population, the high cost of health care and family care for the disease, and other economic and health consequences.	16
Generalisability	21	Discuss the generalisability (external validity) of the study results We are using a nationally representative sample (MHAS), a well-developed microsimulation model (FEM) and the analysis is based in a strong conceptual model, so we could conclude that our results may be generalizable to other populations with high prevalence/incidence of diabetes and an accelerated aging process.	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based This study was funded by grants from the National Institute on Aging. The funders had no input into the selection or analysis of data or the content of the final manuscript.	

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.



BMJ Open

Projecting diabetes prevalence among Mexicans aged 50 years and older: The Future Elderly Model-Mexico (FEM-Mexico)

Journal:	BMJ Open
Manuscript ID	bmjopen-2017-017330.R2
Article Type:	Research
Date Submitted by the Author:	22-Aug-2017
Complete List of Authors:	Gonzalez Gonzalez, Cesar; Universidad de Colima, Facultad de Trabajo Social Tysinger, Bryan; University of Southern California Goldman, Dana; University of Southern California Wong, Rebeca; University of Texas, Department of Preventive Medicine and Community Health
Primary Subject Heading :	Diabetes and endocrinology
Secondary Subject Heading:	Public health, Health economics
Keywords:	General diabetes < DIABETES & ENDOCRINOLOGY, HEALTH ECONOMICS, PUBLIC HEALTH

SCHOLARONE™ Manuscripts

Projecting diabetes prevalence among Mexicans aged 50 years and older: The Future Elderly Model-Mexico (FEM-Mexico)

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

School of Social Work, University of Colima, Mexico, Cesar Gonzalez-Gonzalez professor Roybal Center for Health Policy Simulation, University of Southern California, Bryan Tysinger director

Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Dana P Goldman director,

Sealy Center on Aging, University of Texas Medical Branch, Rebeca Wong professor

Corresponding author: C Gonzalez-Gonzalez cgonzalez31@ucol.mx

Abstract

Objective Diabetes has been growing as a major health problem and a significant burden on the population and on health systems of developing countries like Mexico that are also aging fast. The goal of the study was to estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes.

Design A simulation study using longitudinal data from three waves (2001, 2003 and 2012) of the Mexican Health and Aging Study (MHAS) and adapting the Future Elderly Model (FEM) to simulate four scenarios of hypothetical interventions that would reduce diabetes incidence, and to project the future diabetes prevalence rates among populations 50 years and older.

Participants Data from 14,662 participants with information on self-reported diabetes, demographic characteristics, health and mortality.

Outcome measures We obtained, for each scenario of diabetes incidence reduction, the following summary measures for the population aged 50 and older from 2012-2050: prevalence of diabetes, total population with diabetes, number of medical visits.

Results In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico; 19.3% had been diagnosed with diabetes; and the 2001-2003 diabetes incidence was 4.3%. The no-intervention scenario shows that the prevalence of diabetes is projected to increase from 19.3% in 2012 to 34.0% in 2050. Under the 30% incidence reduction scenario, the prevalence of diabetes will be 28.6% in 2050. Comparing the no-intervention scenario with the 30% and 60% diabetes incidence reduction scenarios, we estimate a total of 816,320 and 1.6 million annual averted cases of diabetes, respectively, for the year 2020.

Discussion Our study underscores the importance of diabetes as a disease by itself, but also the potential health care demands and social burden of this disease and the need for policy interventions to reduce diabetes prevalence.

Strengths and limitations of this study

- The study is the first in Mexico using national representative longitudinal-individual data to project the prevalence of diabetes among older adults in Mexico.
- The study uses an adapted version of the Future Elderly Model, a demographic and economic simulation model designed to project the future costs and health status of the elderly based on their recent past and current health status and taking into account a broad set of risk factors.
- Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes.
- The limitations are related to the nature of the data from the Mexican Health and Aging Study, since the analysis is based on self-reported data and may underestimate the prevalence of diabetes. The Future Elderly Model is using only two waves of information to estimate the disease transitions, and this could have an impact on the reliability of results.

Introduction

Diabetes represents a major health problem and a significant burden on health care systems and societies overall. This is particularly the case in countries like Mexico, where the prevalence of diabetes among the population 20-79 years old was 15.9% in 2011. This was the highest in the OECD (1) and ranked No. 9 worldwide (2). According to the national estimates in Mexico, the self-reported prevalence of diabetes among the population aged 60 and older was 24% in 2012, and in the period between 2000 and 2012 the prevalence doubled among those aged 70 and older from 10% to 20%, and among those aged 60-69 the prevalence grew 1.5 times, going from 18% to 26% (3).

Population aging and the growing prevalence of diabetes raise concerns about the increased burden on social, health and family systems because of the known consequences of this disease. People with diabetes may experience additional health complications (4) (5), greater social needs (6), loss in productivity and earnings (7) and diminished quality of life (8) (9). Moreover, in 2012, diabetes was the leading cause of mortality in the Mexican adult population, accounting for 17% of all deaths (10). It is also the leading cause of premature withdrawal from economic activity, blindness and renal failure (11). Diabetes has a direct impact not only on overall life expectancy but also on the quality of life of the older adult population.

A key risk factor associated with diabetes is high body weight (12), as obese or overweight individuals are more likely to become diabetic (13). Estimates from the 2012 National Health Survey in Mexico reveal that 41% of adults aged 30-49 were overweight, 37% obese and 79% had abdominal obesity (14); figures are similar for those aged 50 years and older (3). Furthermore, obesity is projected to increase across all age groups, with serious implications for diabetes patients and for the Mexican health care system (2).

From a public policy perspective, it is important to take a glance into the future burdens and understand how the prevalence of diabetes will change over the next decades. Moreover, since there are health interventions that have proven to be effective in reducing the onset and management of the disease, it is important to understand how current and potential new policies, particularly those designed to prevent or ameliorate the rise of chronic diseases, may alter the

diabetes trends. For sure, the future prevalence of diabetes will be influenced by the momentum of population aging, the trends in obesity and the patterns of medical advances, among other factors. Thus, we estimate the future cases of diabetes among older adults in Mexico, assuming the current patterns of risk factors and behaviors, as well as the likely trends if hypothetical preventive interventions are adopted to reduce the onset of new cases.

One way to assess the future burden of the disease is to use microsimulation models. Projecting the prevalence of diabetes, the number of diabetics in the population and the consequences for the health care system in terms of health care needs can be useful for public health policy makers, in order to raise awareness of the potential consequences of varying paths that the burden of diseases can take, and possibly designate resources to prevent cases. Microsimulation has been used as a tool for social science research and policy analysis (15), and can be used to evaluate the impact of interventions under alternative scenarios (16). Such scenarios often rely on information from clinical trials where evidence strongly supports the ability to prevent or delay the onset of a disease. For example, a systematic review of the literature concludes that a variety of interventions can help reduce the onset and improve the management of diabetes in a diversity of country settings. This review takes into account the costs involved as well (17). Specifically for the United States, the Diabetes Prevention Program (DPP) was a multicenter randomized clinical trial that demonstrated that weight loss through dietary changes and more physical activity could prevent or delay onset of Type 2 diabetes, resulting in 58% reduction in the incidence of diabetes. The DPP also showed that use of a generic oral diabetes drug (metformin) reduced the incidence of disease among at-risk individuals by 31%. Thus, for the purposes of this paper, we consider the future prevalence of diabetes if it were possible to adopt hypothetical public health interventions that reduced the incidence of diabetes on a scale up to the results shown by the DPP (18). We selected these results for simulation of the scenarios, with the caveat that these results might not perfectly apply to Mexico. We are assuming average effectiveness of national-level interventions, which may be difficult to achieve, but the assumed scenarios can help policy makers understand the impact on the burden of diabetes if these various levels of prevention could be achieved, including the projected burden should no intervention be adopted.

The goal of the study was to estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes. We estimate future levels of diabetes under different scenarios for the population aged 50 years and older in Mexico. Were hypothetical interventions to be implemented to reduce the incidence of diabetes, the two main questions we answer are: how much would the prevalence of diabetes change? And how would the health care burden of diabetes diminish, in terms of medical resources to treat the disease?

To address these questions, we modeled the trajectory of future diabetes in Mexico from 2012 to 2050 using a microsimulation model, the Future Elderly Model (FEM). We construct four scenarios for the projections, estimating the effect of reducing two-year diabetes incidence rates by 0%, 10%, 30% and 60%. We selected the scenarios based on evidence from clinical trials, with effects from as large as that in the clinical trial setting to more attenuated. The microsimulation model takes into account the current prevalence, the estimated new cases of diabetes (incidence) among those aged 50 and older in each two-year period, the deaths among the group 50 and older in each two-year period in the future.

Using information on what can be achieved by implementing proven interventions helps us to construct different scenarios that reflect realistic results of adopting these interventions. Combining results from clinical trials, past trends based on national health surveys and individual characteristics from the MHAS could lead to stronger conclusions about the future of diabetes in Mexico.

Methods and data

The FEM is a demographic and economic simulation model, originally designed to project the future costs and health status of the elderly based on their current health status and taking into account a broad set of risk factors (19). In contrast to projection models that use aggregate measures of health traits for a population cohort, the FEM uses information on how individual health characteristics change at the individual level using longitudinal survey data (20). Details on the FEM have been described elsewhere (21).

The individual level data comes from the Mexican Health and Aging Study (MHAS), a prospective survey of a nationally and urban–rural representative sample of adults aged 50 years and older residing in Mexico in 2001 (22). From its inception, the MHAS was designed to be highly comparable to the U.S. Health and Retirement Study (HRS). The MHAS content includes health in multiple domains, health behaviors and risk factors, socioeconomic conditions, work history, health insurance, health expenditures and family background, among others. A next-of-kin module gathers information on deceased study participants. We used three waves of available data: 2001, 2003 and 2012. A refresher sample of individuals aged 50-61 was added in 2012, to once again represent the population aged 50 and older in 2012.

For our purposes, FEM-Mexico uses two main modules of the FEM developed for the U.S. (FEM-US). The first produces individual trajectories, that is, 2 year transitions, and estimates incidence for a number of health conditions and disability statuses. The second module ensures that the data remains representative of the population aged 50 years and older into the future by replenishing the sample, with 50-51 year olds incorporated into the sample every two years.

The data used for the FEM-US and the FEM-Mexico differ in one important methodological aspect, the inter-wave periods. As mentioned above, the FEM was created to be used with the U.S. Health and Retirement Study (HRS), a longitudinal survey collected every two years; MHAS has a two-year gap between the first (2001) and second (2003) wave, and a 9-year gap between the second and third (2012) wave. To overcome this methodological difference, we use the MHAS 2001 and 2003 waves to estimate health transitions and two-year incidence, and we use the 2012 wave as the baseline to start the microsimulation. In other words, we imposed the 2001-2003 health transitions onto the 2012 MHAS population. We tested the adequacy of this approach by applying the 2001 prevalence and the 2001/2003 incidence to project the prevalence of diabetes in 2012. We then compared the estimated prevalence with the prevalence observed in MHAS 2012 and the estimates were quite similar; hence, we concluded that this approach is reasonable. These results are not shown but are provided in the Technical Appendix.

To measure diabetes prevalence, MHAS respondents were asked: "Has a doctor or medical personnel ever told you that you have diabetes or a high blood sugar level?" The equation for the 2001 to 2003 diabetes incidence was used to estimate the probability of developing diabetes, using a probit regression model with covariates measured in 2001 as follows: age (50-64, 65-74, 75+ years), gender (male, female), education (less than basic, basic, high school and college), marital status (single, married, separated/divorced, widowed), ever hypertension (yes, no), body mass index (BMI underweight/normal, overweight, obese¹), smoking status (never, current, or former), physical activity in the last two years (yes, no), size of locality of residence (less than 100,000 inhabitants, 100,000 or more inhabitants) and health insurance (yes, no). To estimate the incidence equation, only the cases that reported no diabetes in 2001 are included in the analytical sample.

We estimated similar incidence equations using probit regression models for self-reported hypertension heart attack, lung disease, stroke and mortality; ordered probit models for smoking status (never, current, former), limitations with five Activities of Daily Living (ADL's) (none, one, two, three or more) and four Instrumental Activities of Daily Living (IADL's) (none, one, two or more) and linear regression models for log (BMI). The list of variables included in the right-hand-side of each equation varies depending on the theoretical relationship of the independent variables with the corresponding dependent variable.

Since FEM works as a simultaneous equations model, the parameters in one equation affect the parameters of the other equations, meaning that transitions could occur in multiple diseases in any given year of the projection. Thus, an individual could have more than one disease transition in the same year, e.g., new diabetes and new hypertension. Similar to FEM-US, in FEM-Mexico, once a health condition (chronic disease) is acquired or mortality occurs, these states are treated as absorbing or permanent.

In addition, we assessed the health-care consequences of diabetes by comparing in each one of the scenarios the number of medical visits by diabetics *versus* non-diabetics. We estimated an OLS equation for the number of medical visits as a dependent variable, including

¹ Underweight/normal is defined as a BMI lower than 25, overweight is defined as a BMI between 25.0 and 29.9 and a BMI of 30 or higher is considered obese.

with/without diabetes as the main explanatory variable. MHAS respondents were asked: "In the last year, how often have you visited or consulted a doctor or medical personnel?"

To maintain representativeness of the 50 year and older population, the microsimulation model needed replenishment cohorts every two years. To replenish the sample, we took the sample of 50/51 year olds that were added to the sample from MHAS 2012. Then, the model applied the predicted probabilities of health transitions and the health status of the new 50/51 year cohorts to the sample of individuals in the MHAS 2012 to calculate the future health status. This process was repeated every two years in the projections until 2050, and then summary variables were calculated.

Since we anticipated that the new cohorts in the future are going to have different characteristics than the current ones, we calculated and applied trends for diabetes prevalence, BMI and smoking status using data on younger cohorts from an alternative source of information, the Mexican National Health and Nutrition Surveys (ENSA 2000 and ENSANUT 2006 and 2012), a series of repeated national cross-sections in Mexico. Based on the observed/predicted characteristics (education, BMI, smoking) of the younger cohorts who will enter ages 50/51 in the future, we anticipate that future 50/51 year olds will have higher prevalence of diabetes, overweight and obesity, and also higher education than the current 2012 cohort. These trends are not shown but are available from the Technical Appendix

We implemented the FEM-Mexico simulation by loading the 50+ MHAS population in 2012, then applying the two-year transition models for mortality and incidence of health conditions (diabetes, other comorbidities, ADL's, IADL's, BMI and smoking status) with Monte Carlo decisions to calculate the new states of the population every two years. We estimated the total population by adjusting for immigration and mortality forecasts using data from the Mexican National Population Council (CONAPO) projections, and added the new 50/51 year olds to the simulation every two years. Finally, summary variables were computed.

We simulated four scenarios for the projected diabetes prevalence rates among the population 50 and older through 2050. We adopted these scenarios to estimate the potential benefits of prevention programs (20) according to the results from (23) about the efficacy of

alternative interventions, for example by changing lifestyle and using prescription drugs: 1) *Status quo*, or no-intervention. This scenario assumes that the current trends will continue, that is, current rates of e.g., smoking, obesity, other diseases, will continue unchanged. 2) 60% reduction in the incidence of diabetes starting at age 50 in 2014, assumed for every cohort entering age 50 in the future. According to the DPP, an intensive lifestyle intervention and medication (e.g., metformin) among high-risk cases could reduce the incidence of diabetes by 60%; thus we simulated a scenario under such assumption. 3) 30% reduction in two-year diabetes incidence, assuming that older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014. 4) a modest 10% reduction in two-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and economic policies are implemented to reduce diabetes risk factors starting at age 50, that, among the entering cohorts, but that the interventions impact the behaviors of all age groups starting in 2014.

The resulting number of diabetes cases for each scenario are used to estimate the consequences of future diabetes in terms of health care resources. We obtain a gross estimate of the total number of medical visits for patients with and without diabetes and, applying the cost of a medical visit, we calculated the corresponding total health care cost. In the results section, first we present the descriptive characteristics of the 50 years and older population in 2012, the starting period of the simulations. Next, we present the incidence of the health conditions between 2001 and 2003, as well as the marginal effects of the covariates for each of the equations but with a special focus on the diabetes equation and diabetes as a covariate in other equations. Finally, we present a summary of projected values for a selection of years between 2012 and 2050.

Results

Table 1 presents descriptive statistics using information just from MHAS. In 2012, there were approximately 20.7 million persons aged 50 and older in Mexico; of these, 19.3% had been diagnosed with diabetes, 37.9% with hypertension, and the prevalence for each of the other diseases (heart attack, stroke, lung disease and cancer) was less than 5%. The percentage of the population reporting difficulty in performing at least one ADL and IADL was 12.8% and 8.9%,

respectively, and the percentage of the population reporting difficulty in performing at least one of either ADL or IADL was 16.6%. Of the total population aged 50 and older, 35.1% had normal weight, 42.8% were overweight and 22.0% were obese. The average age was 62.6 years, 46.9% were men and 53.1% women; almost half of the 50 years and older population reported less than basic schooling (0-5 years), and 1 in 10 had at least some college degree; 70% were married and 15.4% were widowed, with important differences by sex.

The 2001-2003 diabetes incidence was 4.3% and the factors significantly associated with the onset of diabetes were: education, hypertension and BMI. Higher education was associated with lower probability of having a new case of diabetes. However, this likelihood increased by 1.5% for those with hypertension, 0.8% for those living in urban environments, 1.4% for the overweight and 2.7% for the obese population. As a predictor in the equations for other diseases and health outcomes, diabetes had significant effects, increasing the two-year probability of death by 2.1%, and the two-year incidence of the following: hypertension by 3.4%, a heart attack by 0.7% and a stroke by 1.0% (See Table 2).

Regarding the results of the four simulated scenarios, Table 3 provides baseline estimates from MHAS information (2012) and the projections for the years 2020, 2030, 2040 and 2050 of the prevalence of diabetes (see also Figure 1), the total population, the total number of medical visits per year, the number of diabetics and the number of cases averted in comparison to the no-intervention scenario. The no-intervention scenario shows that the population 50 years and older is projected to increase from 20.7 million in 2012 to 48.0 million in 2050, and the prevalence of diabetes from 19.3% to 34.0%. Under the scenario of 30% reduction in two-year diabetes incidence, the total population is projected to increase to 48.6 million in 2050 and the prevalence of diabetes will be 28.6%. The projected reduction in the prevalence of diabetes is 5.4 points and in mortality 552,000 more survivors. An intermediate and perhaps more plausible scenario is the 10% reduction in two-year diabetes incidence. In this scenario, the population in 2050 will be 48.2 million and the prevalence of diabetes will be 32.3%, a 1.7 point reduction of the prevalence when compared with the no-intervention scenario. The 60% diabetes incidence reduction could lead to a 22.8% prevalence of diabetes in 2050 and 49.2 million individuals aged 50 and older.

The average age of death for the population was 75.3 years in 2012. According to the projections of the FEM-Mexico under the no-intervention scenario, the average age at death was 76.7 years in 2050; 76.8 for the scenario of 10% diabetes incidence reduction; 77.0 years for the 30% diabetes incidence reduction scenario; and 77.3 years for the 60% reduction scenario.

We turn now to the economic consequences of diabetes. Since the MHAS has no data available for the average annual cost by disease, we used a rough approximation from two other sources to gauge the difference in cost related to the presence or absence of diabetes. For Mexico and according to Rodriguez-Bolaños (5), in the Mexican Institute of Social Security (IMSS), the annual cost for a patient with diabetes was \$3,193 dollars. On the other hand, the New York State Diabetes Prevention and Control Program estimates that the average cost of a patient with diabetes is 3.5 times greater than for someone without the disease (22). We applied this ratio and obtained an average cost for a patient without diabetes in Mexico of \$912 per year.

Based on this average health care costs of the diabetic and non-diabetic population, using the projected population from the hypothetical scenarios in each group and assuming that the health care cost ratio between the diabetic and non-diabetic population will remain constant over time, we estimated the individual average yearly health care cost for the years 2012 and 2050. For example, in 2012, the total health care cost for the diabetic population was \$12,802 million (4.0 million * \$3,193) and was \$15,247 million (16.7 million * \$912) for the non-diabetic population. Adding these two amounts, we calculated \$28,049 million in total health care cost for the total population. The individual average yearly cost for 2012 was \$1,353, obtained by dividing the total health care cost by the total population (\$28,049/20.7 million). If we estimate the average health care cost at the individual level for the year 2050, in the no-intervention scenario it would be \$1,663 dollars; in the 10% diabetes incidence reduction scenario, it would be \$1,624 dollars; for the 30% reduction, it would be around \$1,544 dollars; and for the 60% reduction, the average health care cost per individual would be \$1,416 dollars (See Table 4). If we multiply the individual average health care cost by the total population, the annual savings can be obtained by comparing the result to the no-intervention scenario, representing \$1,593 million for the 10% diabetes reduction scenario, \$4,849 million for the 30% reduction scenario, and \$10,190 million for the 60% diabetes incidence reduction scenario.

We express these estimates in fiscal terms by estimating the share of the total national health expenditures that the diabetic population represents. According to the World Health Organization Global Health Expenditure database, the total expenditures in health care in Mexico was about \$28,049 million in 2012. Using figures from Table 4, in 2012 the health care cost of the diabetic population represents 45.6% (\$12,802 million /\$28,049 million) of the total health care cost. Similarly, in 2050, due to the increase in the diabetes prevalence and based on the no-intervention scenario, the health care cost of the diabetic population will represent 63.2% of the total. The equivalent share for the 10% reduction scenario would be 61.4%, compared to 57.3% share under the 30% reduction scenario, and for the 60% diabetes incidence reduction scenario, the health care cost of the diabetic population represents 49.8% of the national health care cost.

To supplement the information about the economic consequences of diabetes, we used MHAS data to estimate that, in 2012, the 50 years and older population on average had 4.9 medical visits a year; the average is much higher for individuals with diabetes (8.3) compared to the older adults without diabetes (annual average of 4.1). Our microsimulation estimates are that, in 2050, under the no-intervention scenario, the average number of medical visits would be 6.4 for the older population, 8.8 for individuals with diabetes and 5.2 for those older adults without diabetes, and the increase is mostly related to the presence of diabetes and other health conditions, for example, hypertension.

If we compare the total number of medical visits in each year of the projection for the no-intervention scenario *versus* the 10% reduction in two-year diabetes incidence, we cannot find a large difference. However, if we examine the cumulative number of avoided medical visits from 2012 to 2050, the perspective is quite different. In 2012, a medical visit in the Mexican Institute of Social Security (IMSS) costs 559 pesos (35 US dollars) (24). With the projection results, and assuming that this cost per visit remains the same in constant terms, we can roughly compare the no-intervention with the 30% incidence reduction scenario. We estimate 49.2 million avoided medical visits from 2012 through 2050, which represents \$2,047 million in savings. Similarly, we estimate 547,543 avoided medical visits between 2014 and 2016, representing \$10.4 million dollars in savings (data not shown).

Similarly, we estimate the number of cases that could be averted if we could reduce the incidence/prevalence of diabetes. When comparing the no-intervention scenario to the 30% diabetes incidence reduction scenario (with, say, lifestyle modification), we calculate for the year 2020, a total of 816,320 annual averted cases of diabetes, and for the year 2050, 2.5 million. If we compare no-intervention with the 60% diabetes incidence reduction scenario (with metformin plus lifestyle modifications), the averted cases of diabetes would be 1.6 million in 2020 and 5.4 million in 2050 (see Figure 2).

Discussion

In the present study we projected the diabetes prevalence in Mexico under four scenarios of diabetes incidence reduction: no-intervention, and hypothetical interventions that would reduce incidence 0%, 30% and 60%. Our simulation results, from 2012 through 2050, underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions, which drive a significant rise in health care costs. We provide estimates of the impact that a reduction in the diabetes incidence could represent for the public health system in terms of the amount of population without diabetes and the corresponding savings in health care costs.

The analysis of specific diabetes prevention interventions is beyond the scope of our paper, but previous authors have contributed vastly to this body of evidence. The Diabetes Prevention Program and other research studies using medical trials had found that interventions to reduce the incidence of diabetes could delay the onset of the disease and reduce its prevalence by 10-60% depending on the duration of the interventions and the strategies used, ranging from lifestyle changes to prescribed drugs, or a combination of both. We choose to apply the results from the DPP to the FEM-Mexico scenarios because the program focuses on lifestyle modification and Mexico is promoting public policies to change diet and increase exercise among the population; also, the DPP recommended the use of metformin, a drug proven to delay the onset of diabetes, whose low cost makes it applicable in Mexico. This body of research suggests that public policies could focus on lifestyle modification, weight loss and increased

physical activity to prevent or delay diabetes (25). These clinical trials have identified the variety of interventions and the heterogeneity of their effectiveness; the upper limit of the scenarios we used in our simulations may be difficult to achieve in clinical practice or at the population level because of the heterogeneity in the characteristics and preferences of individuals (26). Nevertheless, the evidence shows that the interventions intended to delay diabetes may result in significant savings if the cost of the intervention were less than the costs treatments. In addition, these studies highlight the importance of interventions that identify individuals at the highest risk of developing diabetes, in order to maximize the effectiveness of interventions and minimize side-effects of interventions with prescribed drugs. While personalized or tailored treatment may not be feasible for the general population as a whole, it could represent great gains if applied to certain population groups: for example, those identified at the highest risk of developing diabetes. Thus, tools to identify those at the highest risk may be highly relevant in countries with limited resources like Mexico. Also, research evaluating the cost and effectiveness of public health interventions aimed at reducing diabetes incidence should be prioritized, as without such information it is not possible at this stage to know if such interventions are likely to reduce the net future healthcare cost, and if so by how much.

Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes. These potential savings represent a rough estimate and may be a lower bound, since we have not considered the benefits of reducing diabetes to the families, economic productivity and the gains in quality of lives of the individuals involved. Certainly, projections such as the ones we present can serve to raise awareness about major trends with population aging that may affect health, and thus social and economic development (27). The projected scenarios illustrate the future burden of the disease if current trends continue unchanged, as well as the potential beneficial effects if interventions to reduce diabetes prevalence are implemented.

The limitations of the study are related to the nature of the data from the Mexican Health and Aging Study. For example, the analysis is based on self-reported data and may not fully represent the prevalence of diabetes (28), and the model's use of only two waves of information to estimate disease transitions may potentially impact the reliability of results.

The acceleration of population aging in the coming decades will play a key role in the burden of the disease (4), as older adults are more likely to develop diabetes than younger adults, and mortality among people with diabetes is declining. These two factors, combined with better technology to manage the disease, may increase the prevalence of diabetes and the years spent with the disease. Obesity trends are also important. The current epidemic of obesity in Mexico implies that the health care system needs to quantify the future high cost of the *status quo*. Our estimates show that, if left unchanged, the prevalence of diabetes will reach unprecedented growth by 2050. Thus, diabetes is projected to be one of the major challenges for the Mexican aging society, given its prevalence, the associated risk factors, the genetic predisposition of the Mexican population, the high cost of health care and family care for the disease, and other economic and health consequences. We hope to have contributed to the knowledge of the potential trends and benefits of diabetes prevention and control interventions that can begin now, and that this information can prove to be of assistance to decision makers.

Contributors: Cesar Gonzalez Gonzalez (CGG), Bryan Tysinger (BT), Rebeca Wong (RW) and Dana P Goldman (DG) made substantial contributions to the conception and design of the paper. BT assisted with analysis and interpretation of data for this manuscript. CGG analyzed the data, and drafted and revised the paper. RW, BT and DG revised the draft paper critically for important intellectual content. All authors approved of the final version to be published. CGG is the guarantor.

Funding: This study was funded by grants from the National Institute on Aging. The funders had no input into the selection or analysis of data or the content of the final manuscript.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: support from the National Institute of Aging (Grants P30AG024968 and R01AG025533); Dr. Goldman is a founder of Precision Health Economics, a consultancy that provides services to the life sciences industry; and no other relationships or activities that could appear to have influenced the submitted work.

Transparency: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data sharing statement: The MHAS is a public use data set that can be obtained from the MHAS webpage http://www.mhasweb.org/

"I Cesar Gonzalez-Gonzalez The Corresponding Author of this article contained within the original manuscript which includes any diagrams & photographs within and any related or stand alone film submitted (the Contribution") has the right to grant on behalf of all authors and does grant on behalf of all authors, a licence to the BMJ Publishing Group Ltd and its licencees, to permit this Contribution (if accepted) to be published in the BMJ and any other BMJ Group products and to exploit all subsidiary rights, as set out in our licence set out at: http://www.bmj.com/about-bmj/resources-authors/forms-policies-and-checklists/copyright-openaccess-and-permission-reuse."

Please tick **one or more** boxes as appropriate:

I am the sole author of the Contribution.
I am one author signing on behalf of all co-owners of the Contribution.
The Contribution has been made in the course of my employment and I am signing as
authorised by my employer.
I am a US Federal Government employee acting in the course of my employment.
I am not a US Federal Government employee, but some or all of my co-authors are.
I am an employee of the UK Crown* acting in the course of my employment
I am a US Federal Government employee acting in the course of my employment.
I am not a US Federal Government employee, but some or all of my co-authors are.
I am an employee of the UK Crown acting in the course of my employment
I am not an employee of the UK Crown acting in the course of my employment but
some/all of my co-authors are.*

Bibliography

- 1. OECD. Cardiovascular Disease and Diabetes: Policies for Better Health and Quality of Care. 2015.
- 2. Arredondo A, De Icaza E. Costos de la Diabetes en América Latina: Evidencias del Caso Mexicano. Value Heal. 2011;14(5 SUPPL.):S85–8.
- 3. Gutiérrez JP, Rivera-Dommarco J, Shamah-Levy T, Villalpando-Hernández S, Franco A, Cuevas-Nasu L, et al. Ensanut 2012Encuesta Nacional de Salud y Nutrición 2012. Resultados Nacionales. [Internet]. Instituto Nacional de Salud Pública. Cuernavaca; 2012. Available from: http://ensanut.insp.mx/informes/ENSANUT2012ResultadosNacionales.pdf
- 4. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr [Internet]. 2010;8(1):29. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20969750%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC2984379
- 5. Rodríguez Bolaños R, Reynales Shigematsu LM, Jimenez Ruiz JA, Juárez Márquez SA, Hernández Ávila M. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2010;28(6):412–20.
- 6. OECD. Projecting OECD Health and Long-Term Care Expenditures: What Are the Main Drivers? 2006.
- 7. Rull J, Aguilar-Salinas C, Rojas R, Rios-Torres JM, Gómez-Pérez FJ, Olaiz G. Epidemiology of type 2 diabetes in Mexico. Vol. 36, Archives of Medical Research. 2005. p. 188–96.
- 8. IDF. Diabetes Atlas. Seventh Edition, 2015.
- 9. Mata M, Antoñanzas F, Tafalla M, Sanz P. El coste de la diabetes tipo 2 en España. Gac Sanit. 2002;16(6):511–20.

- 10. Agudelo-Botero M, Dávila-Cervantes CA. Carga de la mortalidad por diabetes mellitus en América Latina 2000-2011: los casos de Argentina, Chile, Colombia y México. Gac Sanit [Internet]. 2015;29(3):172–7. Available from: http://dx.doi.org/10.1016/j.gaceta.2015.01.015
- 11. Aguilar-Salinas CA. Diabetes y tuberculosis: En el laberinto del subdesarrollo. Rev Investig Clin. 2005;57(1):82–4.
- 12. Bertram MY, Lim SS, Barendregt JJ, Vos T. Assessing the cost-effectiveness of drug and lifestyle intervention following opportunistic screening for pre-diabetes in primary care. Diabetologia. 2010;53(5):875–81.
- 13. Pinto G, Beltrán-sánchez H. Prospective study of the link between overweight / obesity and diabetes incidence among Mexican older adults: 2001-2012. Salud Publica Mex. 2015;57(1):s15–21.
- 14. Rtveladze K, Marsh T, Barquera S, Sanchez Romero LM, Levy D, Melendez G, et al. Obesity prevalence in Mexico: impact on health and economic burden. Public Health Nutr. 2014;17(1):233–9.
- 15. Wolf DA. Synthetic Trajectories obtained by matching longitudinal data. 2014.
- 16. Zucchelli E, Jones A, Rice N. The evaluation of health policies through dynamic microsimulation methods. UK; 2012.
- 17. Li R, Zhang P, Barker LE, Chowdhury FM, Zhang X. Cost-effectiveness of interventions to prevent and control diabetes mellitus: A systematic review. Diabetes Care. 2010;33(8):1872–94.
- 18. Knowler W, Barret-Connor E, Fowler S, Hamman R, Lachin J, Walker E, et al. Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin. N Engl J Med [Internet]. 2002 Feb 7;346(6):393–403. Available from: http://www.nejm.org/doi/abs/10.1056/NEJMoa012512
- 19. Goldman DP, Zheng Y, Girosi F, Michaud PC, Olshansky SJ, Cutler D, et al. The benefits of risk factor prevention in Americans aged 51 years and older. Am J Public Health. 2009;99(11):2096–101.
- 20. Olshansky SJ, Goldman DP, Zheng Y, Rowe JW. Aging in America in the Twenty-First Century: Demographic Forecasts from the MacArthur Foundation Research Network on an Aging Society Published by: Wiley on behalf of Milbank Memorial Fund content in a trusted digital archive. We use information techn. Milbank Q. 2013;87(4):842–62.
- 21. Goldman DP, Lakdawalla D, Michaud P, Eibner C, Zheng Y, Gailey A, et al. The Future Elderly Model: Technical Documentation. 2015.
- Wong R, Michaels-Obregon A, Palloni A. Cohort Profile: The Mexican Health and Aging Study (MHAS). Int J Epidemiol. 2015;1–10.
- 23. Gregg EW, Boyle JP, Thompson TJ, Barker LE, Albright AL, Williamson DF. Modeling the impact of prevention policies on future diabetes prevalence in the United States: 2010-2030. Popul Health Metr. 2013;11(1):18.
- 24. Rodríguez Bolaños RDLÁ, Reynales Shigematsu LM, Jiménez Ruíz JA, Juárez Márquezy

- SA, Hernández Ávila M, Jimenez Ruiz JA, et al. Costos directos de atención médica en pacientes con diabetes mellitus tipo 2 en México: análisis de microcosteo. Rev Panam Salud Pública. 2010;28(6):412–20.
- 25. Guthrie DW. The Prevention or Delay of Type 2 Diabetes. Clin Diabetes. 2002 Jul 1;20(3):109–16.
- 26. Dorresteijn JAN, Visseren FLJ, Ridker PM, Wassink AMJ, Paynter NP, Steyerberg EW, et al. Estimating treatment effects for individual patients based on the results of randomised clinical trials. BMJ. 2011;343:d5888.
- 27. Imhoff E van, Post W. Microsimulation Methods for Population Projection. Popul An English Sel. 2008;10(1):97–138.
- 28. Kumar A, Wong R, Ottenbacher KJ, Al Snih S. Prediabetes, undiagnosed diabetes, and diabetes among Mexican adults: Findings from the Mexican Health and Aging Study. Ann Epidemiol. 2016;26(3):163–70.



Table 1. Characteristics of the population 50 years and older, MHAS 2012

Age (mean) Sex (male)	62.6
Sov (malo)	
Sex (Illaie)	46.9
Education	
Less than complete basic (0 to 5 years)	46.4
Basic complete (6 years)	20.8
High school (7 to 12 years)	22.8
College (13+ years)	10.0
Marital Status	
Single	5.1
Married	69.8
Separated/Divorced	9.6
Widowed	15.5
Chronic diseases (% Yes)	
Hypertension	37.9
Diabetes	19.4
Cancer	1.2
Heart attack	3.0
Lung disease	5.1
Stroke	2.2
Disability (%)	
Any ADL (1+)	12.9
Any IADL (1+)	11.7
Any ADL or Any IADL	19.3
Body Mass Index (BMI)	
Normal (< 25.00 kg/m ²)	35.1
Overweight (25.00 to 29.99 kg/m ²)	42.9

Obese 1 (30.00 to 34.99 kg/m²)	16.7
Obese 2 (35.00 to 39.99 kg/m²)	3.8
Obese 3 (≥40 kg/m²)	1.6
Smoking Status	
Never	63.7
Former	23.4
Current	13.0

Source: MHAS 2012. Weighted statistics.

Table 2: Incidence equations for mortality, chronic diseases, smoking status and BMI for the population 50 years and older, FEM-Mexico 2001-2003 (Marginal effects)

				Heart		Lung		Smoke	Log
	Mortality	Diabetes	Hypertension	attack	Cancer	Disease	Stroke	(Current)	BMI
TWO YEAR INCIDENCE	2.3	4.3	16.1	1.4	0.4	2.7	0.5	8.5	3.3
				Ma	rginal effec	cts			
Lag age 50-64	0.002	-0.001	0.003	0.001	0.000	0.001	0.000	-0.003	0.002
Lag age 65-74	0.001	-0.002	-0.002	0.001	0.000	0.000	0.001	-0.001	-0.004
Lag age 75+	0.003	0.000	-0.001	0.000	-0.001	0.001	0.000	-0.004	0.000
Male	0.017	0.004	-0.049	0.004	0.000	-0.001	-0.001	0.124	-0.004
Basic school	0.005	0.021	-0.039	-0.009	0.005	-0.014		-0.023	0.028
Highschool	0.012	-0.030	-0.005	-0.002	0.006	-0.007	0.005	0.015	0.005
College	-0.013	-0.019	-0.042	0.005	0.006	-0.012	-0.003	0.011	0.012
Lag Hypertension	0.003	0.015		0.016			0.004	-0.036	0.007
Lag Diabetes	0.021		0.034	0.007			0.010	-0.019	-0.003
Lag Heart attack	0.017						0.002	-0.021	0.013
Lag Cancer	0.074						-0.002	-0.010	-0.001
Lag Lung Disease	0.011							0.005	-0.003
Lag Stroke	0.027							-0.025	0.001
Lag 1 IADL	0.001							-0.019	-0.001
Lag 2+ IADL	0.000							-0.036	-0.014
Lag 1 ADL	0.013							0.014	0.001
Lag 2 ADL	0.057							0.035	0.008
Lag 3+ ADL	0.154							0.038	0.014
Lag Former smoker	0.003	-0.010		0.003	0.002	-0.002	0.003		0.002
Lag Widowed	0.012	-0.005		-0.001	-0.002	0.002	-0.001	0.014	0.000
Lag NOT Exercise	0.013	0.008	0.020	0.007	0.001	0.006	0.002	0.120	0.010
More urban locality	0.005	0.007	-0.008	-0.003	0.001	-0.010	0.001	0.014	0.017
Lag BMI less than 30	0.042	0.111	0.114	0.008					0.968
Lag BMI 30 or higher	0.030	0.040	0.186	-0.008					0.616

Table 3: Projection of prevalence of diabetes, total population and number of medical visits by Simulation Scenarios, Population 50 years and older, FEM-Mexico simulation 2012-2050

ESTIMATE by SCENARIO	2000	2006	2012	2020	2030	2040	2050
Diabetes prevalence (%)							
Observed	12.00	15.74	19.34				
No intervention			19.34	26.24	30.69	32.91	34.00
10% incidence reduction			19.34	25.23	29.29	31.29	32.25
30% incidence reduction			19.34	23.32	26.27	27.74	28.64
60% incidence reduction			19.34	20.42	21.35	22.05	22.76
Total Population							
No intervention			20,727,415	26,781,877	34,641,639	41,652,429	48,010,723
10% incidence reduction			20,727,415	26,794,525	34,705,941	41,774,461	48,180,921
30% incidence reduction			20,727,415	26,814,809	34,832,223	42,027,492	48,563,485
60% incidence reduction			20,727,415	26,851,575	35,021,745	42,468,762	49,191,108
Number of medical visits (A	nnual)						
No intervention			102,183,113	151,881,059	216,505,084	274,138,503	324,866,875
10% incidence reduction			102,183,113	151,328,257	215,568,988	273,165,155	323,819,400
30% incidence reduction			102,183,113	150,258,034	213,441,667	270,708,771	321,751,070
60% incidence reduction			102,183,113	148,650,611	209,909,778	267,031,679	318,180,682
Number of diabetics (Annua	I)						
No intervention			4,009,290	7,364,738	11,155,124	14,407,673	17,209,864
10% incidence reduction			4,009,290	7,083,003	10,660,831	13,737,582	16,380,310
30% incidence reduction			4,009,290	6,548,418	9,587,597	12,240,966	14,648,013
60% incidence reduction			4,009,290	5,736,938	7,826,970	9,816,176	11,773,857
Averted cases of diabetes							
(vs. no-intervention)				201 = 2 =	40.4.055	0=0.000	
10% incidence reduction			-	281,735	494,293	670,092	829,554
30% incidence reduction			-	816,320	1,567,527	2,166,708	2,561,851
60% incidence reduction			-	1,627,799	3,328,153	4,591,497	5,436,007

Table 4: Projection of total population, percentage, and health care cost by diabetes status, population aged 50 and older, FEM-Mexico simulation 2012-2050

Characteristics	2012	2050					
Characteristics	2012	No intervention	10% reduction	30% reduction	60% reduction		
Total Population	20,727,415	48,010,723	48,180,921	48,563,485	49,191,108		
Proportion of population by Diabetes diagnosis							
With	19.34	34.00	32.25	28.64	22.76		
Without	80.66	66.00	67.75	71.36	77.24		
Total Population by Diabetes Condition							
With	4,009,290	15,797,928	15,031,288	13,451,263	10,858,373		
Without	16,718,125	32,212,795	33,149,633	35,112,222	38,332,735		
Total Health care costs by diabetes condition							
With	12,801,662,970	50,442,784,104	47,994,902,584	42,949,882,759	34,670,784,989		
Without	15,246,930,000	29,378,069,040	30,232,465,296	32,022,346,464	34,959,454,320		
Total	28,048,592,970	79,820,853,144	78,227,367,880	74,972,229,223	69,630,239,309		
Individual average Health care cost	1,353	1,663	1,624	1,544	1,416		

Figure 1: Diabetes Prevalence for Scenarios of Diabetes Incidence Reduction, Population aged 50 and older, FEM-Mexico 2012-2050

Figure 2. Number of averted DIABETES cases, No intervention scenario vs 30% and 60% diabetes incidence reduction, FEM-Mexico



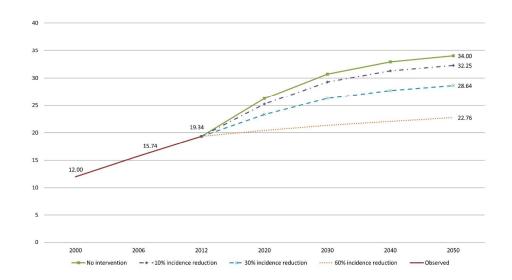


Figure 1: Diabetes Prevalence for Scenarios of Diabetes Incidence Reduction, Population aged 50 and older, FEM-Mexico 2012-2050

338x190mm (300 x 300 DPI)

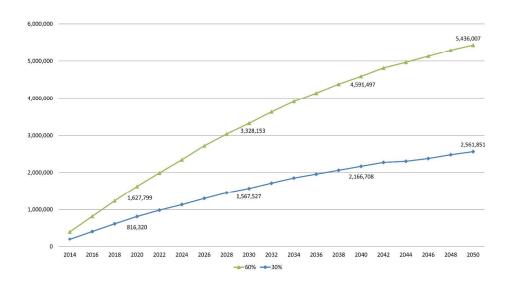


Figure 2. Number of averted DIABETES cases, No intervention scenario vs 30% and 60% diabetes incidence reduction, FEM-Mexico

338x190mm (300 x 300 DPI)

Modeling Diabetes and Related Medical Care of the Future Elderly in Mexico

Cesar Gonzalez-Gonzalez, Bryan Tysinger, Dana P Goldman, Rebeca Wong

Technical Appendix

Structure of the microsimulation model

The structure of the FEM-Mexico microsimulation and the differences with the HRS-FEM are presented in the Appendix Figure 1. Our simulation starts in 2012 with 20.7 Million individuals age 50+ (17.7% of the population in 2012; (CONAPO, 2012)). The simulation model estimates the risk of developing diabetes, other five chronic diseases and the survival status for each individual. Due to the structure of the model, every two years the microsimulation model updates the health status and mortality risk for each individual. To replenish the youngest cohorts, a new cohort of 50 and 51 year-old individuals are added at the beginning of each simulated cycle.

This technical appendix describes only the adaptations made to the FEM in order to work with the Mexican Health and Aging Study (MHAS), in depth details of the FEM are published everywhere (add reference).

The model's main variables are age, gender, smoke, BMI and six chronic conditions (hypertension, diabetes, heart disease, lung disease, stroke and cancer). We also create an indicator variable mortality. The baseline cohort is defined at the initial period (2001). This time period represents the first two years of the simulations (i.e., 2012 and 2013). The variables age, gender, smoke, BMI and chronic conditions are sampled from MHAS with replacement. These samples are repeated until the number of individuals in each age and sex category are equal to the Mexican population distribution in 2012.

After establishing the baseline cohort, the microsimulation iterates to the next time period by projecting the values of each variable for the next two years (i.e., 2014 and 2015). Since the 50 and 51 years individuals age to 52 and 53 years-old, respectively, at time 2, new 50 and 51 year-old individuals are added to the simulation to replenish the youngest age group. The characteristics of these new individuals are sampled with replacement from the 50-51 year-old individuals in MHAS 2012, weighted by the age- and gender-specific projected population of 50 year-olds based on the official Mexican projections (CONAPO) and imposing the trends for some of the main variables.

MHAS provides self-reported chronic conditions for each individual in 2001, 2003 and 2012. We use logistic regressions to estimate the probability of transitioning to one of the six mutually exclusive health states in 2003 based on not having that chronic condition in 2001, controlling for demographic and comorbid conditions in 2001. Then we projected transitions of self-reported diabetes, hypertension, heart attack, cancer, stroke and lung disease. The independent variables

include health status measures and basic demographic characteristics such as age, gender, smoking status or weight category, as measured at baseline in 2001. The coefficient estimates of these transitions models predict health status two years into the future (2003). All chronic conditions are treated as absorbing states.

Specific situations for FEM-Mexico

a. Inter-wave gap period

The first difference between the structure of the FEM-Mexico and the FEM was that in the latter, the main source of information, the Health and Retirement Study (HRS), is collected every two years and the microsimulation uses this gap time to estimate health status of the individuals. In MHAS there is three available waves, 2001, 2003 and 2012 with different inter-wave periods. We had to choose our baseline population based on the advantages that the microsimulation model presents and we decided to use the 2012 data as a baseline and the 2001-2003 information to estimate the health transitions and to run our microsimulation.

b. Cross-validation: Cohort analysis (MHAS 2003-2011/2013)

The next step was to corroborate that adapting the MHAS information to the FEM could lead to acceptable forecast of diabetes, to do so we run a cohort analysis using wave 2 (2003) as the start point of the simulation, then we compare the results obtained from the FEM-Mexico with the real data from MHAS wave 3 (2012). Results show that FEM-Mexico predicts effectively the prevalence of diabetes (see figure 2).

- c. Demographic adjustments to run the simulation
- 1) Since age and sex distribution in the MHAS differs from the CONAPO projections we reweight the population by age and sex to have a common start point for the projections (see Figure 3).
- 2) Using the CONAPO projections (2010-2050) we made some adjustments on mortality probabilities and due to evident differences by age group we adjust for two groups: 50 to 64 years and 65 years and older, all calculations relative to 2012 level (see table 1)
- 3) Migration adjustments [by year (2013-2050) single age and sex], all calculations relative to 2012 level.
 - d. Incoming cohorts (new 50-51 years old)

We assume that the new 50-51 years old individuals will be different in several characteristics. For example, with respect to the actual cohorts, they will be more educated, with lower tobacco and alcohol consumption and with higher BMI. Using information from the Mexican National Health

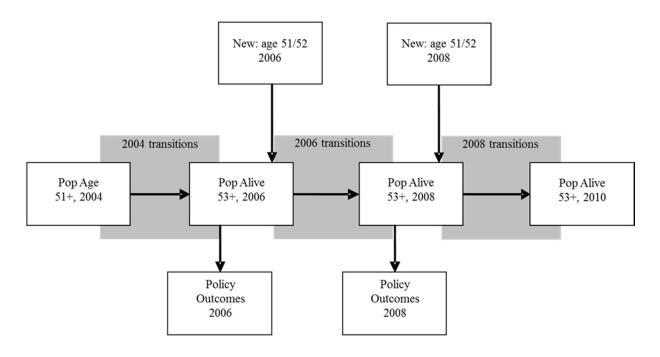
Surveys (2000, 2006 and 2012) we predicted trends for these variables and applied them to the incoming cohorts (50-51 years old).

e. Missing data.

We used records in which the information for all the variables is complete.



Figure 1. **Architecture of the FEM**



HRS-FEM and FEM-Mexico differences

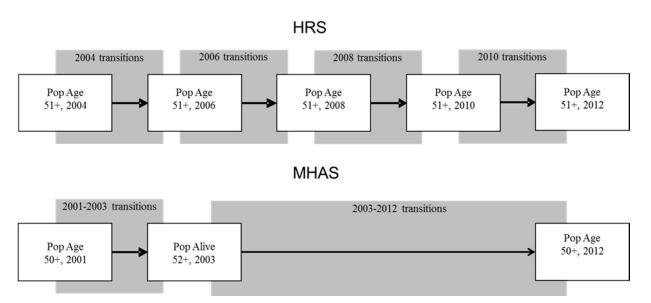
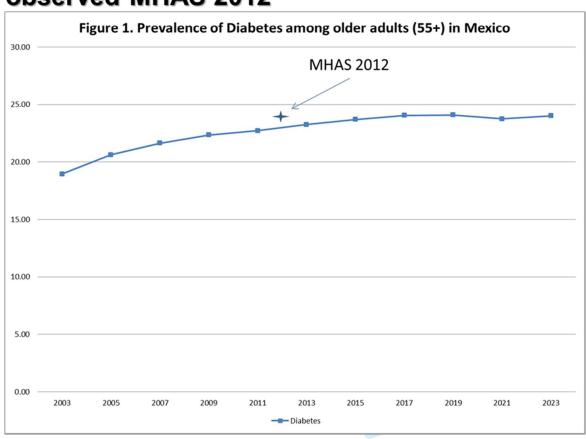


Figure 2.

Comparison between microsimulation and observed MHAS 2012



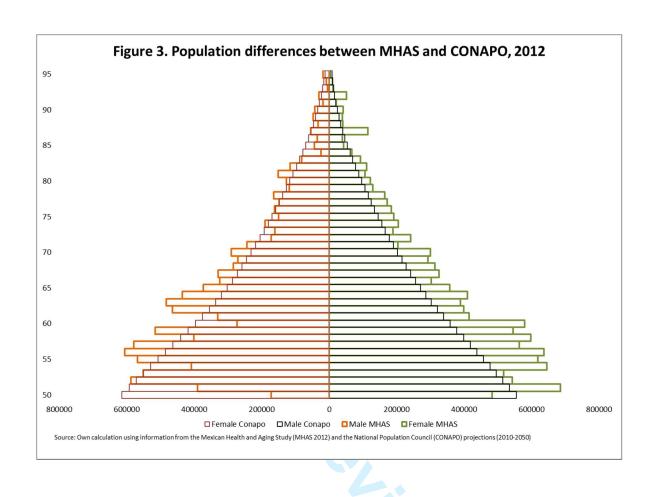


Table 1. Trends for mortality, diabetes, Body Mass Index and Smoking, 2012-2050

Year		Mortality adjustments ¹				rtality adjustments ¹ Diabetes ²		Body Mass Index ²				5	king ²
	50-64	65+	Diabetes	Overweight	Obese 1	Obese 2	Obese 3	Current	Former				
2012	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000				
2013	0.9920	0.9983	1.0176	1.0007	1.0119	1.0196	1.0458	1.0309	0.9856				
2014	0.9838	0.9962	1.0354	1.0014	1.0239	1.0396	1.0935	1.0624	0.9714				
2015	0.9756	0.9934	1.0534	1.0020	1.0359	1.0599	1.1433	1.0947	0.9573				
2016	0.9671	0.9901	1.0718	1.0027	1.0480	1.0806	1.1952	1.1277	0.9434				
2017	0.9585	0.9861	1.0904	1.0034	1.0602	1.1015	1.2492	1.1614	0.9296				
2018	0.9498	0.9817	1.1092	1.0041	1.0725	1.1229	1.3056	1.1959	0.9160				
2019	0.9407	0.9769	1.1283	1.0048	1.0848	1.1445	1.3642	1.2310	0.9026				
2020	0.9317	0.9718	1.1477	1.0055	1.0971	1.1665	1.4253	1.2669	0.8892				
2021	0.9227	0.9666	1.1674	1.0061	1.1096	1.1889	1.4888	1.3035	0.8761				
2022	0.9138	0.9614	1.1873	1.0068	1.1220	1.2116	1.5549	1.3408	0.8630				
2023	0.9051	0.9563	1.2075	1.0075	1.1346	1.2347	1.6237	1.3788	0.8502				
2024	0.8965	0.9515	1.2279	1.0082	1.1472	1.2581	1.6952	1.4175	0.8374				
2025	0.8882	0.9470	1.2487	1.0089	1.1598	1.2819	1.7695	1.4569	0.8249				
2026	0.8802	0.9428	1.2697	1.0096	1.1725	1.3061	1.8467	1.4969	0.8124				
2027	0.8722	0.9388	1.2909	1.0103	1.1852	1.3306	1.9268	1.5377	0.8002				
2028	0.8641	0.9351	1.3125	1.0109	1.1980	1.3555	2.0100	1.5791	0.7880				
2029	0.8561	0.9316	1.3343	1.0116	1.2109	1.3807	2.0964	1.6212	0.7760				
2030	0.8480	0.9282	1.3564	1.0123	1.2238	1.4064	2.1859	1.6640	0.7642				
2031	0.8400	0.9251	1.3788	1.0130	1.2367	1.4324	2.2787	1.7074	0.7525				
2032	0.8319	0.9221	1.4014	1.0137	1.2497	1.4588	2.3749	1.7514	0.7409				
2033	0.8236	0.9195	1.4244	1.0144	1.2627	1.4855	2.4744	1.7960	0.7295				
2034	0.8149	0.9172	1.4476	1.0150	1.2757	1.5126	2.5775	1.8412	0.7182				
2035	0.8058	0.9153	1.4711	1.0157	1.2888	1.5402	2.6841	1.8870	0.7071				
2036	0.7962	0.9138	1.4949	1.0164	1.3019	1.5681	2.7943	1.9334	0.6961				
2037	0.7866	0.9128	1.5189	1.0171	1.3150	1.5963	2.9082	1.9803	0.6852				
2038	0.7766	0.9124	1.5432	1.0178	1.3282	1.6250	3.0259	2.0277	0.6745				
2039	0.7660	0.9125	1.5678	1.0185	1.3414	1.6540	3.1472	2.0757	0.6639				
2040	0.7551	0.9133	1.5927	1.0192	1.3546	1.6835	3.2724	2.1241	0.6535				
2041	0.7439	0.9146	1.6179	1.0198	1.3678	1.7133	3.4015	2.1730	0.6431				
2042	0.7327	0.9163	1.6433	1.0205	1.3811	1.7434	3.5344	2.2223	0.6330				
2043	0.7216	0.9183	1.6690	1.0212	1.3944	1.7740	3.6712	2.2721	0.6229				
2044	0.7106	0.9206	1.6950	1.0219	1.4077	1.8050	3.8119	2.3222	0.6130				
2045	0.6997	0.9234	1.7213	1.0226	1.4210	1.8363	3.9565	2.3727	0.6032				
2046	0.6892	0.9267	1.7478	1.0233	1.4343	1.8680	4.1050	2.4235	0.5936				
2047	0.6791	0.9303	1.7746	1.0239	1.4477	1.9001	4.2574	2.4747	0.5841				
2048	0.6694	0.9340	1.8017	1.0246	1.4610	1.9326	4.4136	2.5261	0.5747				
2049	0.6600	0.9376	1.8290	1.0253	1.4744	1.9655	4.5737	2.5778	0.5654				
2050	0.6517	0.9419	1.8566	1.0260	1.4877	1.9987	4.7376	2.6297	0.5563				

¹ Trends calculated using CONAPO Projections (2010-2050)

 $^{^{\}rm 2}$ Trends calculated using Mexican National Health Surveys (2000, 2006 and 2012)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cross-sectional studies

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	Projecting diabetes among older adults in Mexico: The Future Elderly Model-Mexico (FEM-Mexico)	1
		Objective: To estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health and economic burden of diabetes Design: A simulation study using longitudinal data from the Mexican Health and Aging Study (MHAS) and adapting the Future Elderly Model (FEM) to simulate scenarios of hypothetical interventions that would reduce diabetes incidence. Participants: Data from 14,662 participants with information on self-reported diabetes, demographic and health characteristics, and mortality. Outcome measures: We obtained, for each scenario of diabetes incidence reduction, the following summary measures for the population aged 50 years and older from 2012-2050: prevalence of diabetes, total population with diabetes, number of medical visits Results: In 2012, there were approximately 20.7 million persons aged 50 years and older in Mexico;, 19.3% had been diagnosed with diabetes; and the 2001-2003 diabetes incidence was 4.3%. The no-intervention scenario shows that the prevalence of diabetes is projected to increase from 19.3% in 2012 to 34.0% in 2050. Under the 30% incidence reduction scenario, the prevalence of diabetes will be 28.6% in 2050. Comparing the no-intervention scenario with the 30% and 60% diabetes incidence reduction scenarios, we estimate a total of 816,320 and 1.6 million annual averted cases of diabetes, respectively, for the year 2020. Limitations: The limitations are related to the nature of the data from the Mexican Health and Aging Study, since the analysis is based on self-reported data and maybe underestimate the prevalence of diabetes. Discussion: Our study underscores the importance of diabetes as a disease by itself, but also the potential health care demands and social burden of this disease and the need for policy interventions to reduce diabetes prevalence	2
Introduction			
Background/rationale	2	Diabetes represents a major health problem and a significant burden on health care systems and societies overall. This is particularly the case in countries like Mexico, where the prevalence of diabetes among the population 20-79 years old was 15.9% in 2011. Population aging and the growing prevalence of diabetes raise concerns about the increased burden on social, health and family systems because of the known consequences of this disease –health complications, greater social needs, loss in productivity and earnings and diminished quality of life. From a public policy perspective, it is important to take a glance into the future burdens and understand how the prevalence of diabetes will change over the next decades.	4-5

		One way to assess the future burden of the disease is to use microsimulation models, these models can be used to evaluate	
		the impact of interventions under alternative scenarios.	
Objectives	3	To estimate the future prevalence of diabetes among Mexico's older adults in order to assess the current and future health	6
		and economic burden of diabetes	
Methods			
Study design	4	We modeled the trajectory of future diabetes in Mexico from 2012 to 2050 using a microsimulation model, the Future	6
		Elderly Model (FEM). We construct four scenarios for the projections, estimating the effect of reducing two-year diabetes	
		incidence rates by 0%, 10%, 30% and 60%. We selected the scenarios based on evidence from clinical trials, with effects	
		from as large as that in the clinical trial setting to more attenuated. The microsimulation model takes into account the	
		current prevalence, the estimated new cases of diabetes (incidence) among those aged 50 and older in each two-year	
		period, the deaths among the group 50 and older in each two-year period, and the prevalence among the new population	
		entering the group 50 and older in each two-year period in the future.	
Setting	5	The individual level data comes from the Mexican Health and Aging Study (MHAS), a prospective survey of a nationally and	7
		urban-rural representative sample of adults aged 50 years and older residing in Mexico in 2001. We used three waves of	
		available data: 2001, 2003 and 2012. A refresher sample of individuals aged 50-61 was added in 2012, to once again	
		represent the population aged 50 and older in 2012.	
Participants	6	The baseline survey, in 2001, included a nationally representative sample of Mexicans aged 50 and over and their	7
		spouse/partners regardless of their age. A direct interview was sought with each individual and proxy interviews were	
		obtained when poor health or temporary absence precluded a direct interview.	
Variables	7	To measure diabetes prevalence, MHAS respondents were asked: "Has a doctor or medical personnel ever told you that	8
		you have diabetes or a high blood sugar level?" The equation for the 2001 to 2003 diabetes incidence was used to estimate	
		the probability of developing diabetes, using a probit regression model with covariates measured in 2001: age, gender,	
		education, marital status, ever hypertension, body mass index, smoking status, physical activity in the last two years, size of	
		locality of residence and health insurance. To estimate the incidence equation, only the cases that reported no diabetes in	
		2001 are included in the analytical sample.	
Data sources/	8*	We simulated four scenarios for the projected diabetes prevalence rates among the population 50 and older through 2050.	9
measurement		We adopted these scenarios to estimate the potential benefits of prevention programs (20) according to the results from	
		(23) about the efficacy of alternative interventions, for example by changing lifestyle and using prescription drugs: 1) Status	
		quo, or no-intervention. This scenario assumes that the current trends will continue, that is, current rates of e.g., smoking,	
		obesity, other diseases, will continue unchanged. 2) 60% reduction in the incidence of diabetes starting at age 50 in 2014,	
		assumed for every cohort entering age 50 in the future. According to the Diabetes Prevention Program, an intensive	

Bias		lifestyle intervention and medication (e.g., metformin) among high-risk cases could reduce the incidence of diabetes by 60%; thus we simulated a scenario under such assumption. 3) 30% reduction in two-year diabetes incidence, assuming that older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014. 4) a modest 10% reduction in two-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and	
Bias		older adults receive a structured lifestyle intervention at the national level starting at age 50 in 2014. 4) a modest 10%	
Bias			
Bias		reduction in two-year diabetes incidence also starting at age 50 in 2014. The scenarios assume that environmental and	
Bias			
Bias		economic policies are implemented to reduce diabetes risk factors starting at age 50, that is, among the entering cohorts,	
Bias		but that the interventions impact the behaviors of all age groups starting in 2014.	
	9	We estimated the total population by adjusting for immigration and mortality forecasts using data from the Mexican	9
		National Population Council (CONAPO) projections. For the new cohorts we calculated and applied trends for diabetes	
		prevalence, BMI and smoking status using data on younger cohorts from an alternative source of information, the Mexican	
		National Health and Nutrition Surveys (ENSA 2000 and ENSANUT 2006 and 2012), a series of repeated national cross-	
		sections in Mexico.	
Study size	10	14, 662 individuals with complete information on all the included variables in the analysis. A fixed available sample.	
Quantitative variables	11	The variables in the analysis were coded as follow: age (50-64, 65-74, 75+ years), education (less than basic, basic, high	
		school and college), marital status (single, married, separated/divorced, widowed), body mass index (BMI	
		underweight/normal [lower than 25.0], overweight [25.0-29.9], obese [30 or higher]), smoking status (never, current, or	
		former), size of locality of residence (less than 100,000 inhabitants, 100,000 or more inhabitants), limitations with five	
		Activities of Daily Living (ADL's) (none, one, two, three or more) and four Instrumental Activities of Daily Living (IADL's)	
		(none, one, two or more).	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	6-9
		We used microsimulation models to 1) produce individual trajectories, that is, 2 year transitions, and estimate incidence for	
		a number of health conditions and disability statuses; and 2) ensure that the data remains representative of the population	
		aged 50 years and older into the future by replenishing the sample, with 50-51 year olds incorporated into the sample every	
		two years.	
		We used probit regression models to estimate the probability of developing diabetes. Since the FEM works as a	
		simultaneous equation model we also estimated similar incidence equations using probit regression models for self-	
		reported hypertension, cancer, heart attack, lung disease, stroke and mortality; ordered probit models for smoking status,	
		limitations with five Activities of Daily Living (ADL's) and four Instrumental Activities of Daily Living (IADL's) and linear	
		regression models for log (BMI).	
		We estimated an OLS equation for the number of medical visits as a dependent variable, including with/without diabetes as	
		the main explanatory variable.	
		(b) Describe any methods used to examine subgroups and interactions	

		(c) Explain how missing data were addressed –	
		For BMI - one of the key explanatory variables - we imputed the missing values using STATA.	
		(d) If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed The baseline survey is a national representative survey of individuals born prior to 1951. The baseline survey was conducted in 2001, and a follow-up visit to the same individuals was conducted in 2003. The sample for the MHAS baseline was selected from residents of both rural and urban areas, from the National Employment survey (Encuesta Nacional de Empleo, ENE), carried out by the INEGI (Instituto Nacional de Estadistica y Geografia) in Mexico; 11,000 households with at least one resident of age 50 or older were eligible to be part of the MHAS baseline sample. A follow-up visit was completed in 2012. The sample was refreshed by adding a representative sample of the population from the 1952-1962 birth cohorts, as well as their spouses/partners regardless of age. Similar to the baseline interview, the	
		sampling frame for the new cohort sample was the Mexican National Employment and Occupation Survey (ENOE, previously named National Employment Survey, ENE) 2012. During the 2012 survey, 18,465 interviews were completed, including 2,742 next-of-kin interviews. (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	See Table 1.	21
Outcome data	15*	See Table 3.	23
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included See Tables 2, 3 and 4, and Figures 1 and 2	22-26
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses See Technical appendix	
Discussion			
Key results	18	Summarise key results with reference to study objectives	14

		We projected the diabetes prevalence in Mexico under four scenarios of diabetes incidence reduction: no-intervention, and hypothetical interventions that would reduce incidence by 10%, 30% and 60%. Our simulation results, from 2012 through 2050, underscore the role that diabetes plays as a disease by itself, but also its role in affecting the prevalence of other diseases and health conditions. Our simulations estimate the potential savings to the health care system from reductions in diabetes incidence/prevalence and hence in the total population with diabetes.	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias The limitations of the study are related to the nature of the data from the Mexican Health and Aging Study. For example, the analysis is based on self-reported data and may not fully represent the prevalence of diabetes, and the model's use of only two waves of information to estimate disease transitions may potentially impact the reliability of results.	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Our estimates show that, if left the prevalence of diabetes will reach unprecedented growth by 2050. Thus, diabetes is projected to be one of the major challenges for the Mexican aging society, given its prevalence, the associated risk factors, the genetic predisposition of the Mexican population, the high cost of health care and family care for the disease, and other economic and health consequences.	16
Generalisability	21	Discuss the generalisability (external validity) of the study results We are using a nationally representative sample (MHAS), a well-developed microsimulation model (FEM) and the analysis is based in a strong conceptual model, so we could conclude that our results may be generalizable to other populations with high prevalence/incidence of diabetes and an accelerated aging process.	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based This study was funded by grants from the National Institute on Aging. The funders had no input into the selection or analysis of data or the content of the final manuscript.	

^{*}Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

